Synthetic Studies of Stereoregular Polysaccharides -Influence of Substituent Group on Ring-Opening Polymerization(Dissertation_全文)

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INTRODUCTION

The synthesis of polysaccharides has attracted the attention of investigators for a number of decades. The ultimate aim of such syntheses consists in the creation of a set of synthetic polysaccharides with smoothly and regularly altering structural characteristics that will provide substrates and models for systematic investigations of structure-property relationships for natural polysaccharide chains, studies of their biological function and behavior in a living cell, as well as physico-chemical properties, important from both fundamental and industrial viewpoints.

Regular structures and relative simplicity of repeating units of typical polysaccharides make polycondensation and polymerization the most important synthetic principles rather than stepwise propagation, which is widely applied in peptide or polynucleotide chemistry for the creation of long irregular monomer sequences. The chirality of glycosidic centers in natural polysaccharides determines the strict requirement of stereospecificity of glycosylation reaction chosen for polysaccharide synthesis. [1]

On the other hand, cellulose is the most abundant natural organic polymer, existing as a main plant cell wall component, and is important as a biodegradable and renewable organic material. [2] The study for cellulose, therefore, has been continued for about 150 years, but there are still several problems which should be solved: biosynthesis and biodegradation, crystal structure, chemical synthesis, regiospecific substitution reactions and structure-function relationship of derivatives, and so on. [2, 3] The synthesis of cellulose has been a very important, but extremely difficult problem to be solved, since Schulbach first tried the synthesis. [4]

Recently, Kobayashi and his co-workers reported enzymic synthesis of cellulose. Their synthetic method with cellulase is important and interesting from the standpoint of the first *in vitro* synthesis using an enzyme. [5] Their method, however, does not satisfy the recent demands in molecular design of cellulose derivatives having special functions, because it may not enable special functional groups to be introduced

regiospecifically at the desired hydroxyl groups in the repeating pyranose units of cellulose.

There are many functional cellulose derivatives, cellulose esters and ethers having liquid crystalline properties [6] and chiral recognition ability, [7] sulfonated cellulose with anticoagulant activity like heparin, [8] branched cellulose derivatives with antitumor activity, [9] and so on. However, much remains unknown about the relationship between their structures and properties: which derivatives are more functional or active among those substituted at 2-*O*-, 3-*O*- or 6-*O*-positions. For these studies and for further molecular design of advanced materials from cellulose, it is imperative that we develop methods that make it possible to prepare cellulose derivatives having functional groups at the desired positions among 2, 3, 6-hydroxyl groups in the repeating glucopyranose unit of cellulose.

Polycondensation and ring-opening polymerization methods using a glucose derivative as the starting monomer satisfy the above requirements, [10] but all trials to synthesize cellulose by these methods, attempted since Schulbach first tried, have been unsuccessful. Husemann and Müller, [11] and Hirano [12] reported the condensation of 2,3,6-glucose tricarbanilate with phosphorus pentoxide in a mixture of chloroform / dimethylsulfoxide to give a cellulose-like polymer, being branched and contained about 1 % phosphorus.

Micheel *et al.* [13] and Uryu *et al.* [14] tried cationic polymerization of 1,4-anhydro-2,3,6-tri-*O*-benzyl-α-D-glucopyranose initiated with various Lewis acids, but stereoregular-(1→4)-D-glucopyranan was not obtained. Furthermore, Uryu *et al.* [14] reported the first synthesis of cellulose-type glycopyranan, (1→4)-β-D-ribopyranan by cationic ring-opening polymerization of 1,4-anhydro-α-D-ribopyranose derivatives. Their strategy is not applicable to the synthesis of cellulose, although it is useful for the preparation of a glucan with the same hydroxylation pattern as ribose.

Very recently, Kochetkov described in his review that Malysheva had synthesized completely stereoregular (1→4)-β-glucan from a 1,2-*O*-cyanoethylidene derivative only at high pressure, [10c] but the paper described in detail has not appeared yet.

On the other hand, the syntheses of cello-oligosaccharides have been investigated in the author's laboratory. [16-19] Their studies have clarified the importance of the substituent effect on the glucosylation. It is also important to investigate the substituent effects on the ring-opening polymerization; nobody investigate this problem systematically. This reaction was applied to polysaccharide synthesis only in two series of works, namely on polymerization of sugar anhydrides and internal orthoesters. Cationic polymerization of sugar derivatives is a reaction without direct similarity in low molecular weight carbohydrate chemistry, and presents a unique method of constructing the *O*-glycosidic linkage. [1]

After all, in order to yield cellulose derivatives, the author has investigated ring-opening polymerizations of 1,4-anhydro-α-D-glucopyranose derivatives and α-D-glucopyranose 1,2,4-orthoester derivatives utilizing substituent effects; such a study has not appeared yet. In this thesis, the author focused on the influences of the substituent groups and of the ring-structures on ring-opening polymerizations. In addition, the author discussed methods for synthesizing a (1→5)-β-D-glucofuranan and a (1→4)-β-D-glucopyranan, *i. e.*, cellulose.

In chapter 1, selection and syntheses of 1,4-anhydro-α-D-glucopyranose derivatives, which are the starting materials for cationic ring-opening polymerization, are described.

In chapter 2, the substituent effects on ring-opening polymerization of regioselectively acylated 1,4-anhydro-α-D-glucopyranose derivatives are discussed. Consequently, the author obtains a new non-natural polysaccharide, *i. e.* (1→5)-β-D-glucofuranan.

In chapter 3, selections and syntheses of α-D-glucopyranose 1,2,4-orthoester derivatives, which are the starting materials for cationic ring opening polymerization, are discussed.

In chapter 4, substituent effects on cationic ring-opening polymerization of regioselectively acylated α-D-glucopyranose 1,2,4-orthoester derivatives are

discussed. After all, the author succeeds in the first syntheses of cellulose derivatives, with conversion to cellulose by removal of the protective groups.

The detailed experimental methods and data of compounds are summarized in Experimental Section.

Chapter 1

Selection and Synthesis of 1,4-Anhydro-α-D-glucopyranose Derivatives: Starting Materials for Ring-Opening Polymerization

Introduction

The first attempt to synthesize cellulose *via* ring-opening polymerization of 1,4-anhydro-2,3,6-tri-*O*-benzyl-α-D-glucopyranose was reported by Micheel *et al.* [13] to yield cellulose-like polymer. Uryu *et al.* [14] also tried the polymerization of the same monomer, and obtained stereoregular (1→5)-α-D-glucofuranan, the stereochemistry of which was explained on the basis of the antiperiplanar theory of Deslongchamps *et al.* [20]. Ring-opening polymerization is affected by reaction conditions, and there is a possibility of achieving the chemical synthesis of cellulose by finding the optimum reaction conditions.

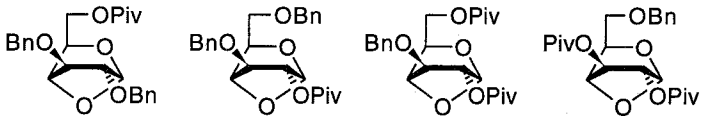
The substituent effects on the stereoselective glycosylation in the syntheses of cello-oligosaccharides have previously been reported. [16-19] Benzyl groups at *O*-3 were indispensable in obtaining β-linked glucosides stereospecifically [17] and the pivaloyl group introduced into *O*-2 lead to a β-linkage by a β-side attack of monomer because of neighboring-group participation [18].

There is a good possibility of synthesizing the expected polysaccharides with both greatly stereo- and regioselectivities by the ring-opening polymerization utilizing such substituent effects. Recently, Ichikawa *et al.* [21] and Kobayashi *et al.* [22] reported the syntheses of (1→6)-β-D-galacto oligosaccharides by applying the neighboring group participation of a 2-*O*-acyl group. There are no papers describing such substituent effects in the ring-opening polymerization of 1,4-anhydro-α-D-glucopyranose derivatives. Therefore, the author studied the substituent effects for the purpose of chemical synthesis of cellulose.

Synthetic methods for the 1,4-anhydro-α-D-glucopyranose derivatives protected with acyl groups have not been reported to date. Reaction conditions for the synthesis

of the 1,4-anhydro-α-D-glucopyranose derivative protected only with benzyl groups [13, 23] reported hitherto were strongly basic. The methods cannot be applied to the preparations of 1,4-anhydro-α-D-glucopyranose derivatives with acyl groups because of the ease of deacylation.

In this chapter, the author describes new synthetic methods for the four compounds protected with acyl groups, 1,4-anhydro-2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose (**1**), 1,4-anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (**2**), 1,4-anhydro-3-*O*-benzyl-2,6-di-*O*-pivaloyl-α-D-glucopyranose (**3**), and 1,4-anhydro-6-*O*-benzyl-2,3-di-*O*-pivaloyl-α-D-glucopyranose (**4**) as starting materials for ring-opening polymerization in order to systematically study the effect of acyl groups on ring-opening polymerization.



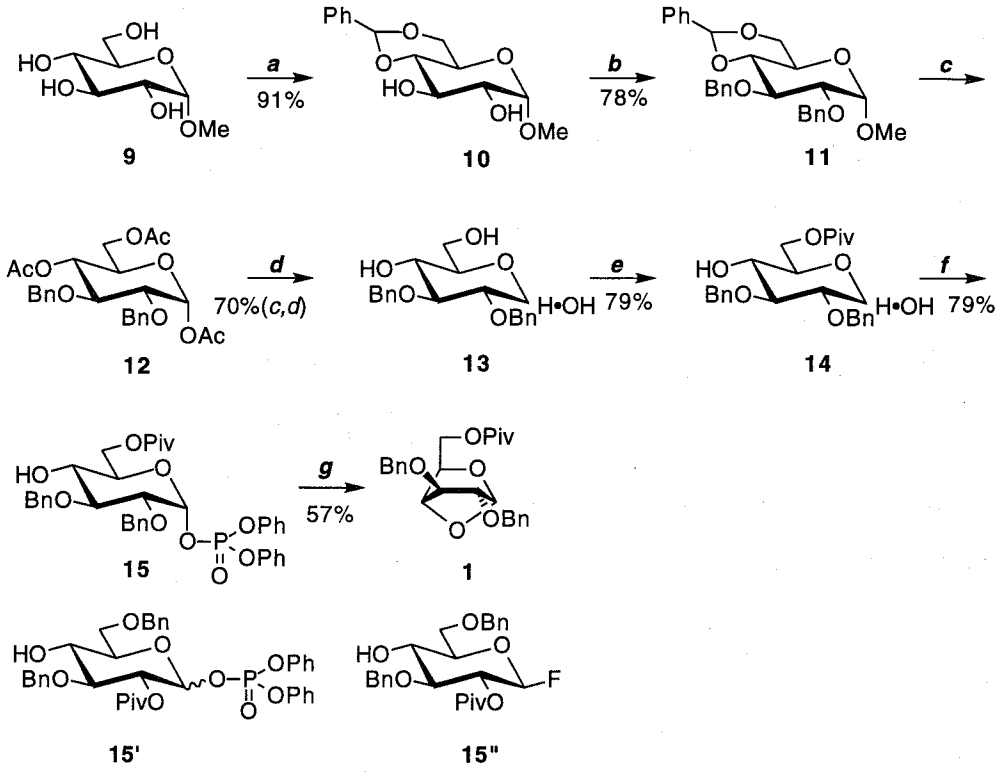
1 **2** **3** **4**

1.1 Synthesis of 1,4-anhydro-2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose (1)

Compounds **1** was prepared according to synthetic route shown in Scheme 1.

Commercially available methyl α-D-glucopyranoside (**9**) was converted to methyl 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-α-D-glucopyranoside (**11**) by 4,6-*O*-benzylidenation and subsequent benzylation in a 71% yield. Demethylation and debenzylidenation with aqueous (aq.) hydrochloric acid in 1,4-dioxane at 100 °C afforded 2,3-di-*O*-benzyl-D-glucopyranose (**13**) in a 39% yield, together with debenzylated by-products. The yield of **13** was improved by the following two reaction steps. Compound **11** was treated with sulfuric acid / acetic anhydride to gave 1,4,6-tri-*O*-acetyl-2,3-di-*O*-benzyl-α-D-glucopyranose (**12**) and then, with sodium methoxide to afford **13** in a 70% overall yield from compound **11**. Selective 6-*O*-pivaloylation of **13** with pivaloyl chloride in pyridine at room temperature provided 2,3-di-*O*-benzyl-6-*O*-pivaloyl-D-glucopyranose (**14**) in a 79% yield. Compound **14** was found to be mono-pivaloylated at the 6-*O*

position from the ^{1}H-NMR (proton nuclear magnetic resonance) analysis: the ratio of the peak areas of aromatic to methyl protons was ten to nine, and both signals of C-1 and C-4 protons were shifted to down-field by the acetylation of **14**.



[a] p-TsOH / $PhCH(OCH_3)_2$ / DMF /40°C / 15 mmHg /1h, [b] NaH / BnBr / DMF / $(n\text{-}C_4H_9)_4NI$ / 0°C
[c] H_2SO_4 / Ac_2O / 0°C [d]NaOMe / MeOH:CH_2Cl_2 (1:4, v/v) [e]PivCl / pyridine / r.t.
[f] BuLi / anhydrous THF / $(PhO)_2POCl$ / -70°C [g]TMSOTf / anhydrous CH_2Cl_2 / 0°C /1.5h

Scheme 1. Synthetic route for compound 1.

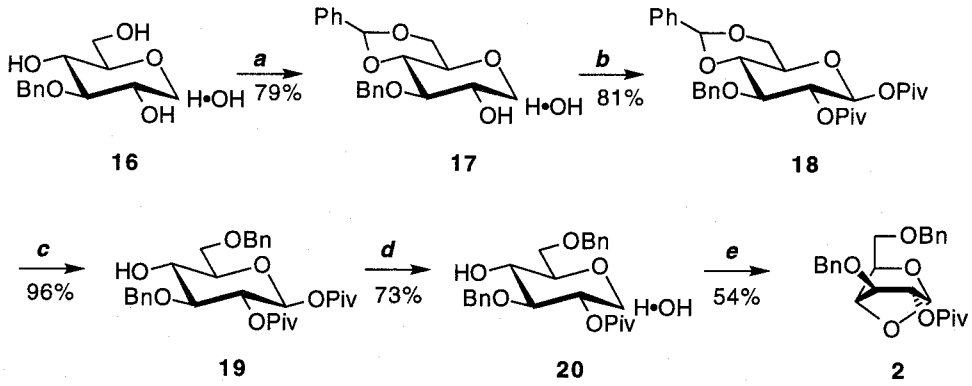
1,4-anhydro-2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose (**1**) was obtained from **14** by a modified method of Hashimoto *et al.* [26]. Compound **14** was first converted *in situ* to its 1-*O*-lithium salt by the treatment of *n*-butyllithium (1.1 equivalent (eq.)), and treatment of the 1-*O*-lithium salt with diphenylphosphorochloride gave 2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranosyl diphenylphosphate (**15**). Compound **15** was so sensitive to moisture at higher temperature that it had to be dried below 0 °C *in vacuo*, and then converted

immediately to **1** in the presence of trimethylsilyl triflate (TMSOTf) (0.1 eq.) at 0 °C in a 57% yield.

Hashimoto *et al.* [26] reported that the glycosidation proceeded *via* the thermodynamically more stable α-ion pair consisting of a pyranoxonium ion and phosphate anion-TMSOTf complex followed by the backside attack with alcohols on this intermediate selectively to give β-glycoside. The mechanism could not apply to the present case, and the following reaction mechanism of the intramolecular glycosylation may be proposed. The carbonyl oxygen at *O*-6 attacks the thermodynamically stable α-ion pair from the β-side to form a carboxonium-ion intermediate, and then the hydroxy group at C-4 attacks C-1 from the opposite side of the intermediate to give the 1,4-anhydro-α-D-glucopyranose derivative.

1.2 Synthesis of 1,4-anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (2)

Compounds **2** was prepared according to synthetic route shown in Scheme 2.



[a] p-TsOH / $PhCH(OCH_3)_2$ / DMF /40°C / 15 mmHg /1h, [b] PivCl / pyridine /80°C,
[c] $NaBH_3CN$ / TMSCl / M.S.4A / CH_3CN / r.t. / 1.5h, [d] $NH_2NH_2•H_2O$ / THF /r.t. / 18h,
[e] p-TsOH / benzene / reflux / 6.5h

Scheme 2. Synthetic route for compound 2.

3-*O*-Benzyl-D-glucopyranose (**16**) [17] was converted to 3-*O*-benzyl-4,6-*O*-benzylidene-1,2-di-*O*-pivaloyl-β-D-glucopyranose (**18**) by benzylidenation and subsequent pivaloylation. Reductive cleavage of the 4,6-*O*-benzylidene acetal derivative (**18**) was performed with sodium cyanoborohydride and trimethylsilyl

chloride in acetonitrile to afford 3,6-di-*O*-benzyl-1,2-di-*O*-pivaloyl-β-D-glucopyranose (**19**) in a 96% yield. 4-*O*-Benzyl derivatives expected from Johansson and Samuelsson's experiments [27] were not obtained. ^{1}H-NMR spectrum of acetylated **19** showed that a signal of a C-4 proton shifted down-field: compound **19** had a free hydroxy group at C-4.

In the case of the reductive cleavage of 4,6-*O*-(4-methoxybenzylidene) acetals of hexopyranosides [27], 4-*O*-(4-methoxybenzyl) derivatives have been reported to be produced regioselectivity with trimethylsilyl chloride as an acidic catalyst. Johansson and Samuelsson [27] stated that the regioselectivity is attributable to the coordination of trimethylsilyl chloride with the oxygen at the C-6 position because of a large steric hindrance at the C-4 position.

The simultaneous presence of molecular sieves 4Å and water was indispensable because the reaction did not proceed without molecular sieves 4Å and also in anhydrous acetonitrle. Probably, molecular sieves 4Å play an important role as a catalyst producing hydrogen chloride from trimethylsilyl chloride and water, and not as a dehydrating agent. Consequently, hydrogen chloride is assumed to be a crucial catalyst, which coordinates with the oxygen at the C-4 position more electron rich than that at the C-6 position in the present reductive ring-opening of benzylidene acetals.

A selective depivaloylation of **19** at the C-1 position was achieved with 4 eq. hydrazine hydrate in tetrahydrofuran at room temperature to give 3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (**20**). In its ^{1}H-NMR spectrum, a shift of a proton at C-1 to up-field indicated that the pivaloyl group only at C-1 was eliminated.

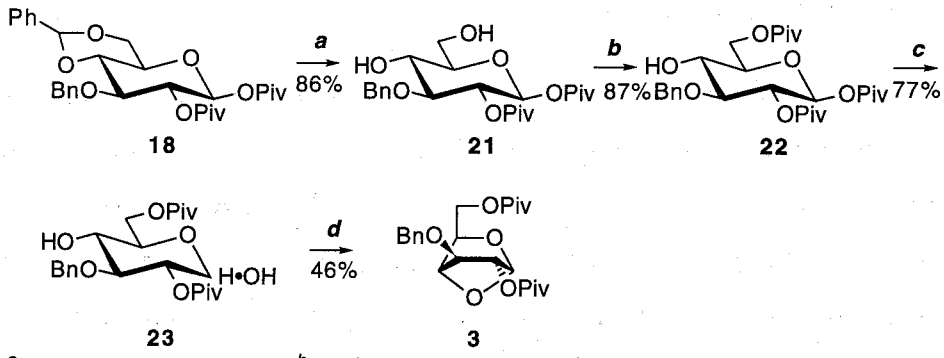
Ring-closure of **20** to **2** was attempted under various conditions. Compound **20** gave a mixture of α-, β-phosphates **15'** (α / β = 1 / 1 by thin layer chromatography (TLC)) by the phosphate method applied to the synthesis of **1**. However, compound **15'** did not afford **2**. β-D-Glucopyranosyl fluoride derivative **15"** synthesized from the corresponding α-chloride derivative [14, 23] did not afford **2**. The ring-closure is difficult

because neighboring-group participation of an acyl group at *O*-2 is prior to the α-side attack of C-4 oxygen on C-1 at low temperature.

Compound **20** was converted to **2** by a large dilution method. This intramolecular dehydration with *p*-toluenesulfonic acid in refluxing benzene increased with a decrease in the concentration of **20**. Compound **2** was obtained in a 54% yield by the reaction conditions described in the experimental section.

1.3 Synthesis of 1,4-anhydro-2,3-di-*O*-pivaloyl-6-*O*-benzyl-α-D-glucopyranose (3)

Compounds **3** was prepared according to synthetic route shown in Scheme 3.



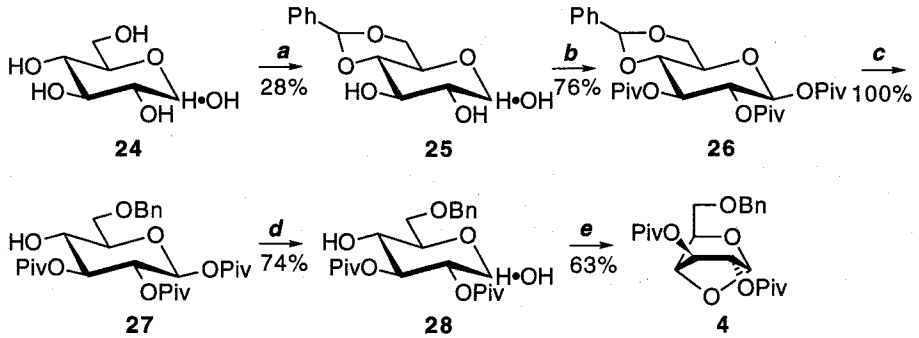
[a] p-TsOH / MeOH / r.t. / 3h, [b] PivCl / pyridine / r.t. / 3h, [c] $NH_2NH_2•H_2O$ / 1,4-dioxane / 50°C 15h, [d] p-TsOH / benzene / reflux / 23h

Scheme 3. Synthetic route for compound 3.

3-O-Benzyl-4,6-*O*-benzylidene-1,2-di-*O*-pivaloyl-β-D-glucopyranose (**18**) was converted to 3-*O*-benzyl-1,2-di-*O*-pivaloyl-β-D-glucopyranose (**21**) by debenzylidenation. Selective 6-*O*-pivaloylation of **21** with pivaloyl chloride in pyridine at room temperature provided 3-*O*-benzyl-1,2,6-tri-*O*-pivaloyl-β-D-glucopyranose (**22**) in a 87% yield. A selective depivaloylation of **22** at the C-1 position was achieved by the same method as that described for the synthesis of compound **20** to give 3-*O*-benzyl-2,6-di-*O*-pivaloyl-D-glucopyranose (**23**) in a 77% yield. Compound **23** was converted to **3** by also the same method as that described for the synthesis of compound **2** in a 46% yield.

1.4 Synthesis of 1,4-anhydro-2,3-di-*O*-pivaloyl-6-*O*-benzyl-α-D-glucopyranose (4)

Compounds **4** was prepared according to synthetic route shown in Scheme 4.



[a] $C_6H_5CH(OMe)_2$ / DMF / 50°C / 15 mmHg / 40 min

[b] PivCl / pyridine / 80°C / 12h, [c] $NaBH_3CN$ / TMSCl / M.S.4A / CH_3CN / r.t. / 1.5h,

[d] $NH_2NH_2 \cdot H_2O$ / THF / 50°C / 51h, [e] p-TsOH / benzene / reflux / 51h

Scheme 4. Synthetic route for compounds 4.

D-Glucose (**24**) was converted to 4,6-*O*-benzylidene-D-glucopyranose (**25**) by benzylidenation. Pivaloylation of compound **25** was performed with pivaloyl chloride at 80 °C to afford 4,6-*O*-benzylidene-1,2,3-tri-*O*-pivaloyl-β-D-glucopyranose (**26**) in a 76% yield. Compound **26** was converted to 6-*O*-benzyl-1,2,3-di-O-pivaloyl-β-D-glucopyranose (**27**) in a *ca.* 100% yield as described for the synthesis of **19**. A selective depivaloylation of **27** at the C-1 position was achieved by the same method as described for the syntheses of compound **20** and **23** to give 6-*O*-benzyl-2,3-di-*O*-pivaloyl-D-glucopyranose (**28**) in a 74% yield. Compound **28** was converted to **4** in a 63% yield by also the same method as described for the syntheses of compound **2** and **3**.

1.5 Summary

In this chapter, the author described synthetic routes for novel compounds **1**, **2**, [24] **3**, and **4** [25] having an acyl group. Compounds **1**, and **2** have one acyl group at C_6-, and C_2-position, respectively. On the other hand, Compounds **3**, and **4** have two acyl groups at C_2- plus C_6-positions, and C_2- plus C_3-positions, respectively. Compounds

1, **2**, [24] **3**, and **4** [25] were given in 57%, 54%, 46%, and 63% yield, respectively. The author's method for obtaining 1,4-anhydro-α-D-glucopyranose derivatives is a large dilution one with a mild acidic condition, which causes intramolecular bond formation. The assignments of proton peaks are summarized in Table 1. A resonance of proton attached to a carbon, to which pivaloyl group is introduced, is shifted to a lower magnetic field.

These routes were important for yielding polysaccharides which had a functional group regiospecifically. In a next chapter, the author describes polymerization of these monomers **1**, **2**, [24] **3**, and **4** [25].

Table 1. ^{1}H-NMR Chemical Shifts of 1,4-Anhydro-α-D-glucopyranose Derivatives

carbon no.	1	2	3	4	5	6		R_2	R_3	R_6
1	5.46	3.70	4.05	4.66	4.0-4.1	4.47	4.55	Bn	Bn	Piv
2	5.41	4.78	3.9-4.0	4.67	4.16	3.86	3.96	Piv	Bn	Bn
3	5.43	4.80	3.97	4.68	4.09	4.45	4.59	Piv	Bn	Piv
4	5.46	4.74	4.93	4.81	4.19	3.70	3.82	Piv	Piv	Bn

CHAPTER 2

Ring-Opening Polymerization of 1,4-Anhydro-α-D-glucopyranose Derivatives

Introduction

Synthetic approach to cellulose *via* ring-opening polymerization of 1,4-anhydro-2,3,6-tri-*O*-benzyl-α-D-glucopyranose was for the first time reported by Micheel *et al.* [13] to yield a cellulose-like polymer. Uryu *et al.* [14] also tried the polymerization of the same monomer, but obtained an unexpected stereoregular (1→5)-α-D-glucofuranan, with stereochemistry elucidated on the basis of the antiperiplanar theory of Deslongchamps. [20] Since 1,4-anhydro-α-D-glucopyranose, which may also be regarded as 1,5-anhydro-β-D-glucofuranose, has two ring-opening modes, that is, 1,4- or 1,5-ring scission, there are four possible structural units in the polymer obtained, which are caused by the ring-opening modes and anomeric α- and β-configurations. Ring-opening polymerization is affected by reaction conditions, and there is a possibility to achieve the chemical synthesis of cellulose by finding optimum reaction conditions.

In the author's laboratory, the substituent effects on the stereoselective glycosylation in the syntheses of cello-oligosaccharides have been studied. [17, 18] The benzyl group at *O*-3 was indispensable to obtain β-linked glucosides stereospecifically [17] in high yield and the pivaloyl group introduced into the *O*-2 led to β-glycosidic linkage by the β-side attack of glycosyl acceptor because of the neighboring-group participation. [17]

There is a possibility to synthesize the expected (1→4)-β-D-glucan with both stereo- and regioregularities by the ring-opening polymerization utilizing such substituent effects. In fact, Ichikawa *et al.* [21] and Kobayashi *et al.*, [22] recently, reported the syntheses of (1→6)-β-D-galacto oligosaccharides by applying the neighboring group participation of the 2-*O*-acyl group. There are no papers describing

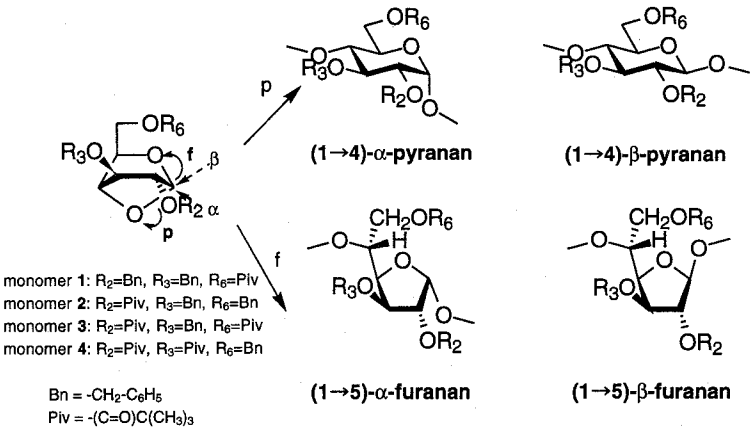
such substituent effects in ring-opening polymerization of 1,4-anhydro-α-D-glucopyranose derivatives.

In the previous chapter, the author described the synthesis of four novel compounds, 1,4-anhydro-2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose (**1**), 1,4-anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (**2**), [24] 1,4-anhydro-3-*O*-benzyl-2,6-di-*O*-pivaloyl-α-D-glucopyranose (**3**), and 1,4-anhydro-6-*O*-benzyl-2,3-di-*O*-pivaloyl-α-D-glucopyranose (**4**) [25] for the purpose of chemical synthesis of cellulose. Compounds **1** and **2** may be expected to give regioselective 1,4-pyranan by the electron-withdrawing acyl group at 6-*O* position, and to induce stereoselective β-glycosidic bond formation by the neighboring group participation of 2-*O*-acyl group, respectively. In addition, polymerization of compound **3** may clarify an influence of a combined effect of 2-*O*-, and 6-*O*-acyl group. A substituent effect at C_3-position (an effect of 3-*O*-benzyl group) may be clarified by the difference in results between polymerizations of **4** and those of monomers **1**, **2**, and **3**.

In this chapter, utilizing such substituent effects in the ring-opening polymerizations of 1,4-anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (**2**) and 1,4-anhydro-3-*O*-benzyl-2,6-di-*O*-pivaloyl-α-D-glucopyranose (**3**), the author describes the first preparation of a stereoregular (1→5)-β-D-glucofuranan, [28] and substituent effects at the 2-*O*, 3-*O*, and 6-*O* positions on ring-opening polymerization for obtaining cellulose by chemical synthesis.

2.1 Ring-opening polymerization of 1,4-anhydro-α-D-glucopyranose derivatives

In general, there are four possible structural units in the poly(D-glucose) prepared *via* ring-opening polymerization of 1,4-anhydro-α-D-glucopyranose derivatives, namely, the (1→4)-β- ((1→4)-β-P) and (1→4)-α-D-glucopyranosidic ((1→4)-α-P) units and the (1→5)-β- ((1→5)-β-F) and (1→5)-α-D-glucofuranosidic ((1→5)-α-F) units (Scheme 5). The structures of these synthetic glucans were determined by means of polarimetry and ^{13}C-NMR spectroscopy.



Scheme 5. Ring-opening modes of 1,4-anhydro-α-D-glucopyranose derivatives.

2.1.1 Determination of structure of poly(1)s synthesized from 1

All poly(**1**)s are dextrorotatory, as shown in Table 2. Taking into account the high positive specific rotation, the poly(**1**) may be a (1→5)-α-D-glucofuranan derivative or a (1→4)-α-D-glucopyranan derivative, *i. e.*, an amylose derivative. The method and logic, which were used for the assignment of four peaks appearing in the ^{13}C-NMR spectrum of an anomeric peak of poly(**1**), were the same as that used by Uryu *et al.* [14]

^{13}C-NMR spectra of poly(**1**)s synthesized from **1** are shown in Figure 1. In spectrum (Figure 1A) of poly(**1**) having $[\alpha]_D$ +83.7° (Table 2, experiment no. 7), the anomeric peak appeared as almost a single peak at 100.2 ppm. In order to assign the peak at 100.2 ppm, the poly(**1**) having $[\alpha]_D$ +83.7° was desubstituted and acetylated. The anomeric peak of acetylated poly(**1**) appeared at 100.4 ppm, which is distinctly different from the 95.7 ppm of amylose acetate. [29] On the other hand, the anomeric peak of cellulose acetate, *i. e.*, a (1→4)-β-D-glucopyranan derivative, appears at 100.5 ppm. [26] However, the cellulose acetate has $[\alpha]_D$ -21° [30], which is distinctly different from $[\alpha]_D$ +109° of the acetylated poly(**1**). Therefore, the anomeric peak at 100.2 ppm was assigned to (1→5)-α-F units.

Spectrum (Figure 1B) of poly(**1**) (Experiment no. 4) shows the four anomeric peaks consisting of 96.7, 100.2, 102.4, and *ca.* 107 ppm. The C-1 peaks of the non-reducing end group of two dimeric model compounds, namely, maltose and cellobiose derivatives [17] with the same protective group system as that of poly(**1**)s, appeared at 96.7 and

Table 2

Polymerization of 1,4-Anhydro-2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose

Experiment No.	initiator	concn, mol %	solv	monomer/solv, g/100mL	temp, °C	time, h	yield, %	10^{-3} M_{GPC}	$\overline{DP_n}$	$[\alpha]_D$, deg	polymer structure, % [a] (1-5)- α-F	(1-5)- β-F	(1-4)- α-P	(1-4)- β-P
1	PF_5	40	CH_2Cl_2	100	-78	189	74	8.1	18.9	+94.9	58	0	42	0
2	PF_5	20	CH_2Cl_2	100	-78	192	56	7.0	16.6	+82.1	44	0	46	10
3	PF_5	5	CH_2Cl_2	100	-78	192	54	9.4	22.1	+90.2	42	0	41	17
4	PF_5	20	CH_2Cl_2	50	-30	252	88	4.0	9.5	+78.4	54	16	22	8
5	PF_5	5	CH_2Cl_2	100	-30	191	83	12.5	29.3	+86.6	72	0	22	6
6	PF_5	20	CH_2Cl_2	50	0	252	80	4.2	9.8	+68.2	37	14	32	17
7	PF_5	5	CH_2Cl_2	100	0	229	62	7.2	16.8	+83.7	ca. 100	0	trace	trace
11	PF_5	20	toluene	50	-30	262	64	4.9	11.5	+77.2	62	trace	17	21
12	PF_5	5	toluene	50	-30	233	18	4.9	11.6	+108	91	0	9	trace
14	$BF_3 \cdot Et_2O$	5	CH_2Cl_2	100	-30	238	78	15.0	35.2	+65.7	55	6	24	15
16	$SbCl_5$	5	CH_2Cl_2	100	-30	166	72	5.8	13.6	+56.7	71	16	0	13

[a] Determined from the proportion of anomeric peaks in ^{13}C-NMR spectrum of Poly(**1**).

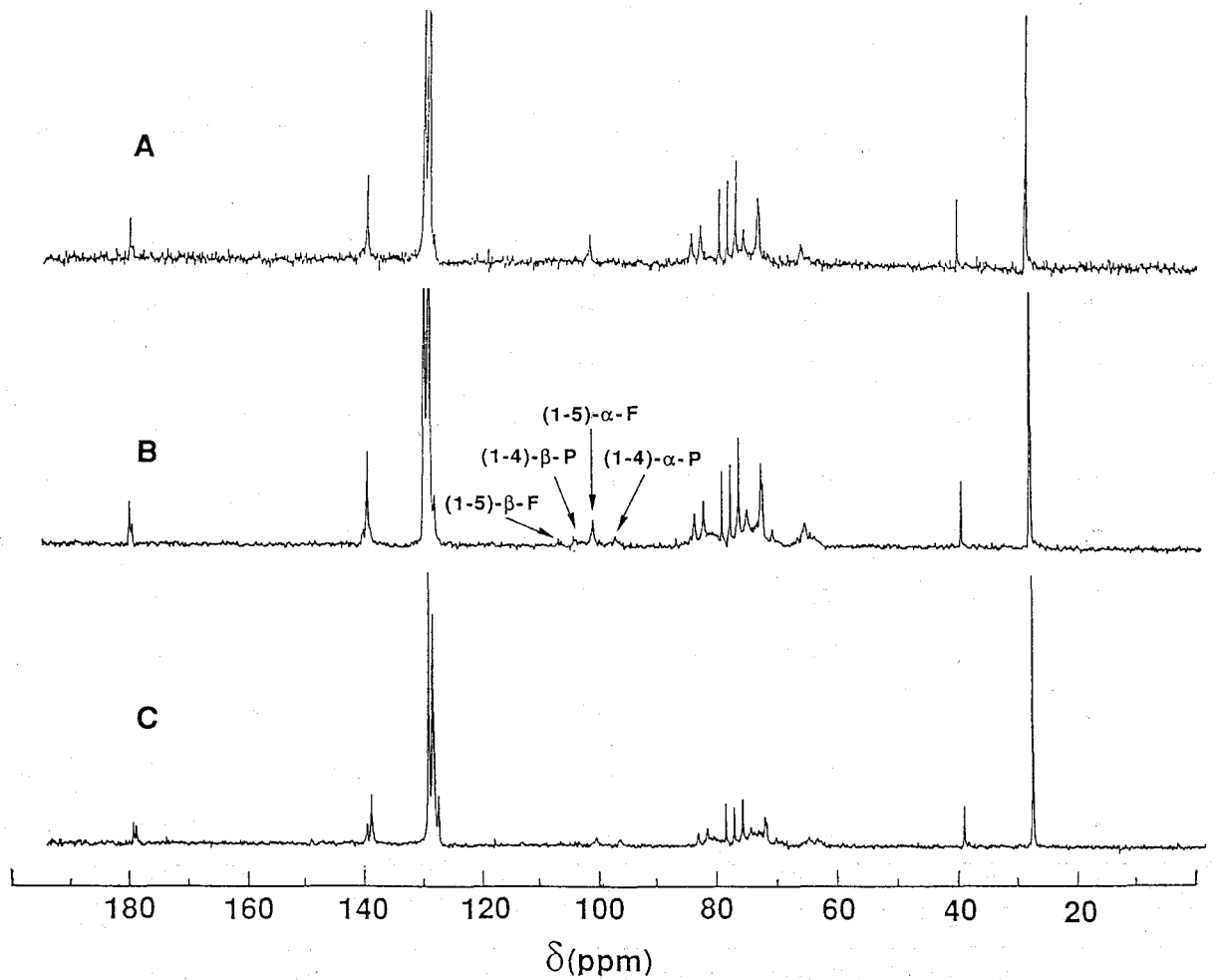


Figure 1. 22.5 MHz ^{13}C-NMR spectra of (A) poly(**1**) prepared by PF_5 at 0°C (Table 2, experiment no. 7), (B) poly(**1**) prepared by PF_5 at -30°C (Table 2, experiment no. 4), (C) poly(**1**) prepared by PF_5 at -78°C (Table 2, experiment no. 1) ($CDCl_3$ as solvent).

102.4 ppm, respectively, so the anomeric peaks of poly(**1**)s at 96.7 and 102.4 ppm were assigned to (1→4)-α-P and (1→4)-β-P units, respectively. Then, the fourth anomeric peak at *ca.* 107 ppm was assigned to (1→5)-β-F units. In spectrum C in Figure 1, poly(**1**) had a structure consisting of (1→4)-α-P and (1→5)-α-F units at -78 °C.

It turned out that stereoregularities were affected by the catalysts used, concentration of the catalyst, and reaction temperature, as shown in Table 2. The production of (1→5)-α-F units increased with a decrease of concentration of PF_5 catalyst. Phosphorus pentafluoride, boron trifluoride etherate and antimony pentachloride gave relatively highly stereoregular poly(**1**)s. Trifluoromethanesulfonic anhydride, which served as a good catalyst for stereoregular polymerization of 1,3-anhydro-β-D-glucopyranose derivative, [31] did not cause stereoregular polymerization of **1**.

None of these conditions, however, gave a completely stereoregular polymer. The difference between our present results and those of Uryu *et al.* [14] is the production of (1→4)-α-P units at -78 °C. This fact clearly indicates that the neighboring participation of 6-*O*-pivaloyl groups affects the structures of poly(**1**)s.

2.1.2 Determination of structure of poly(2)s synthesized from 2

All poly(**2**)s are levorotatory, as shown in Table 3. Taking into account the high negative specific rotation, the poly(**2**)s may be (1→5)-β-D-glucofuranan derivatives or (1→4)-β-D-glucopyranan derivatives.

^1H- and ^{13}C-NMR spectra of poly(**2**) having $[\alpha]_D$ -69.3° are shown in Figures 2 and 3, respectively. These spectra indicate that the poly(**2**) has a high degree of stereoregularity. The anomeric peak of stereoregular poly(**2**) appeared at 108 ppm as a sharp singlet. In order to determine the structure of the stereoregular poly(**2**), it was desubstituted and acetylated. The anomeric peak of the acetylated poly(**2**) appeared at 106.2 ppm. On the other hand, anomeric peaks of cellulose acetate, *i.e.*, a (1→4)-β-D-glucopyranan derivative and amylose acetate, *i.e.*, a (1→4)-α-D-glucopyranan

Table 3

Polymerization of 1,4-Anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose

Experiment No.	initiator	concn, mol %	solv	monomer/solv, g/100mL	temp, °C	time, h	yield, %	10^{-3} M_{GPC}	DP_n	$[\alpha]_D$, deg	polymer structure, % [a] (1-5)- α-F	(1-5)- β-F	(1-4)- α-P	(1-4)- β-P
21	PF_5	15	CH_2Cl_2	50	-30	22	54	3.8	8.9	-57.1	0	ca. 100	0	0
22	PF_5	10	CH_2Cl_2	50	-30	21	80	7.3	17.1	-66.2	0	ca. 100	0	0
23	PF_5	5	CH_2Cl_2	50	-30	34	87	9.4	22.0	-66.9	0	100	0	0
24	PF_5	5	CH_2Cl_2	33	-30	23	61	6.7	15.8	-65.1	0	100	0	0
25	PF_5	5	CH_2Cl_2	25	-30	27	71	5.3	12.4	-63.7	0	100	0	0
26	PF_5	1	CH_2Cl_2	50	-30	39	13	7.3	17.2	-61.2	0	100	0	0
30	PF_5	5	toluene	100	-30	32	65	12.8	30.1	-69.1	0	100	0	0
31	PF_5	5	toluene	50	-30	25	100	13.0	30.8	-69.3	0	100	0	0
32	PF_5	1	toluene	50	-30	38	60	18.1	42.6	-61.2	0	100	0	0
36	PF_5	5	CH_2ClCH_2Cl	50	-30	41	86	7.3	17.1	-64.6	0	100	0	0
37	PF_5	5	CH_3NO_2	50	-28	27	52	8.0	18.7	-76.0	0	100	0	0
40	$BF_3 \cdot Et_2O$	5	CH_2Cl_2	50	-30	60	78	7.5	17.6	-69.3	0	100	0	0
41	$SbCl_5$	5	CH_2Cl_2	50	-30	20	100	3.4	8.1	-65.6	0	100	0	0

[a] Determined from the proportion of anomeric peaks in ^{13}C-NMR spectrum of poly(**2**).

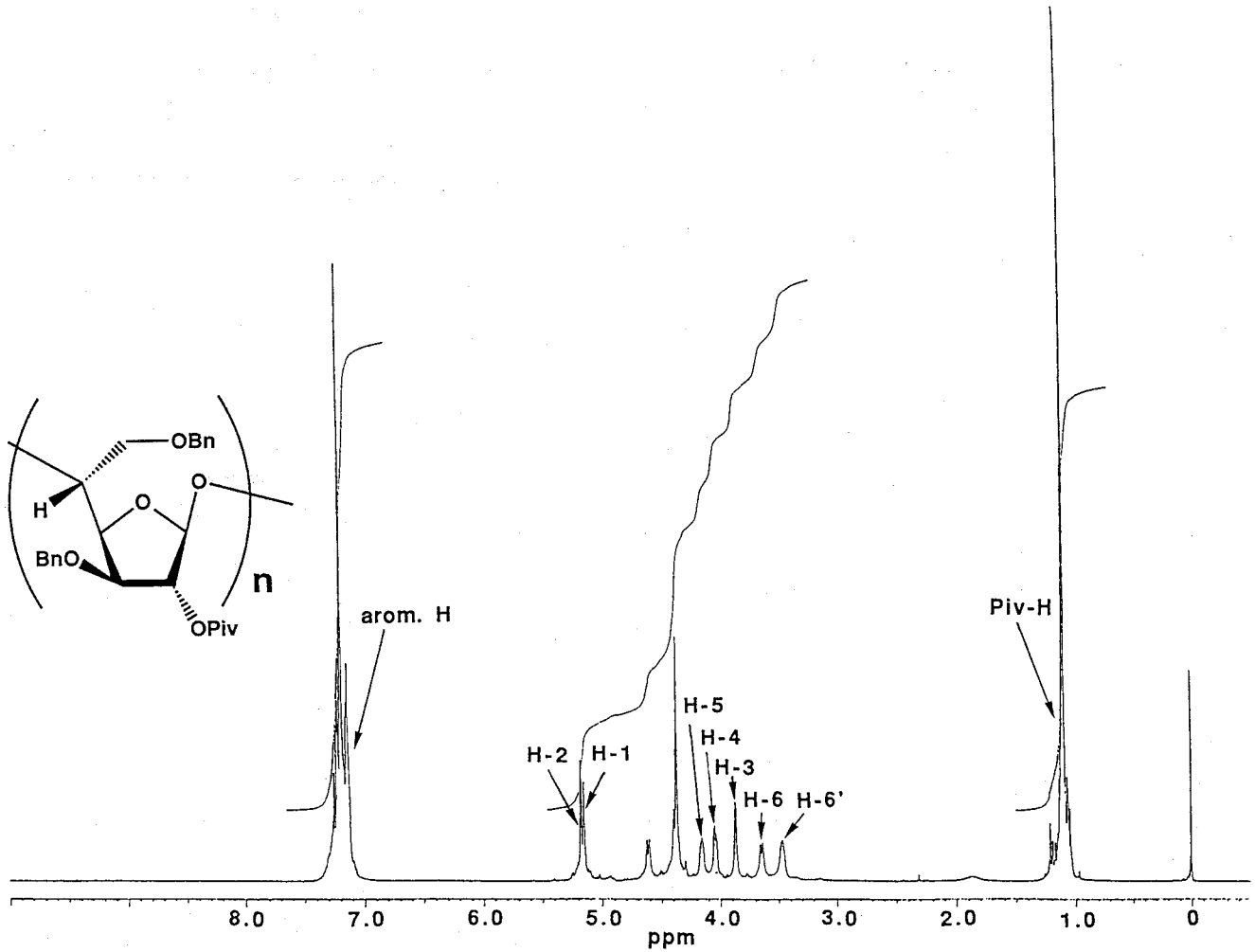


Figure 2. 500 MHz ^{1}H-NMR spectrum of 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan ($CDCl_3$ as solvent).

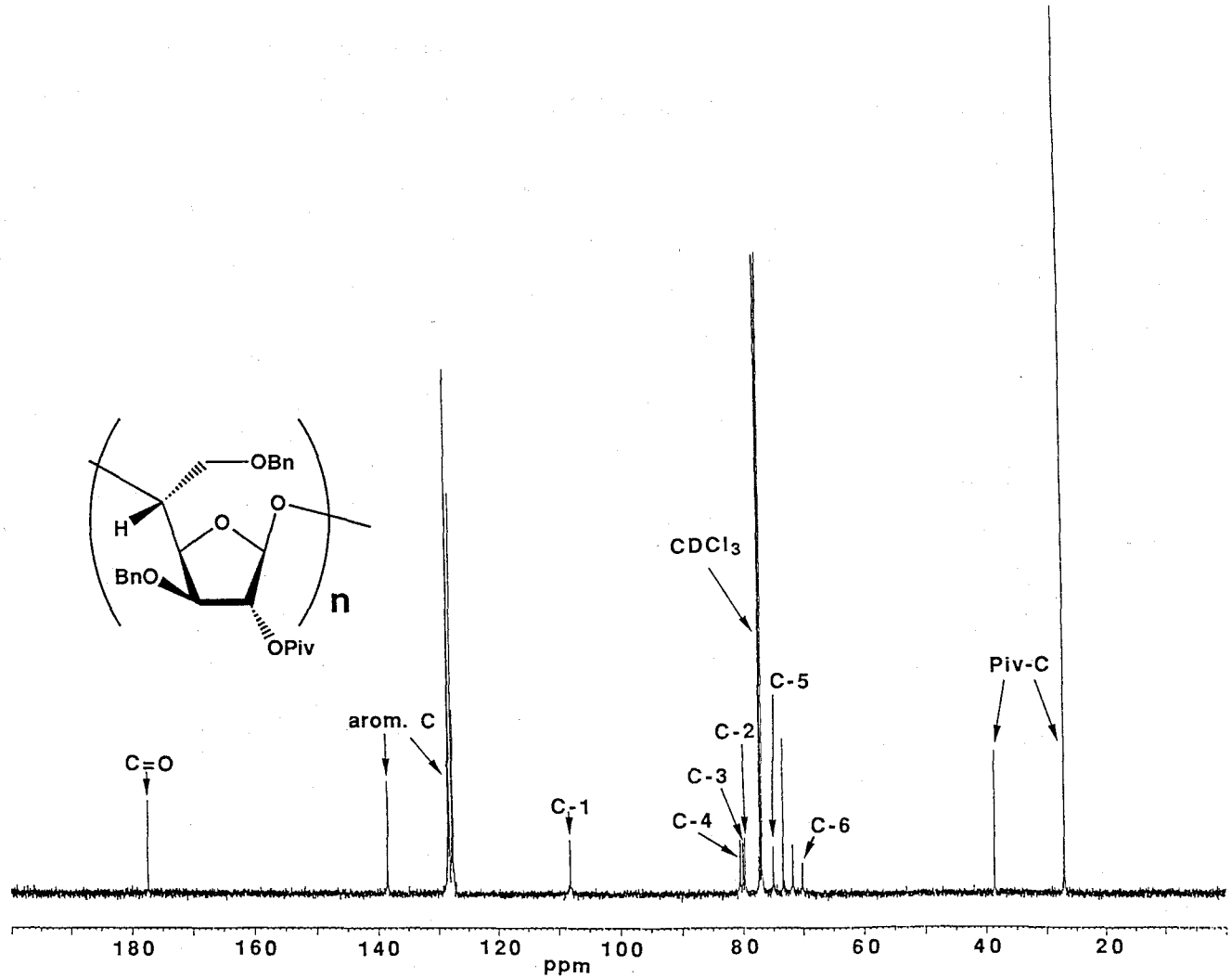


Figure 3. 125 MHz ^{13}C-NMR spectrum of 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan ($CDCl_3$ as solvent).

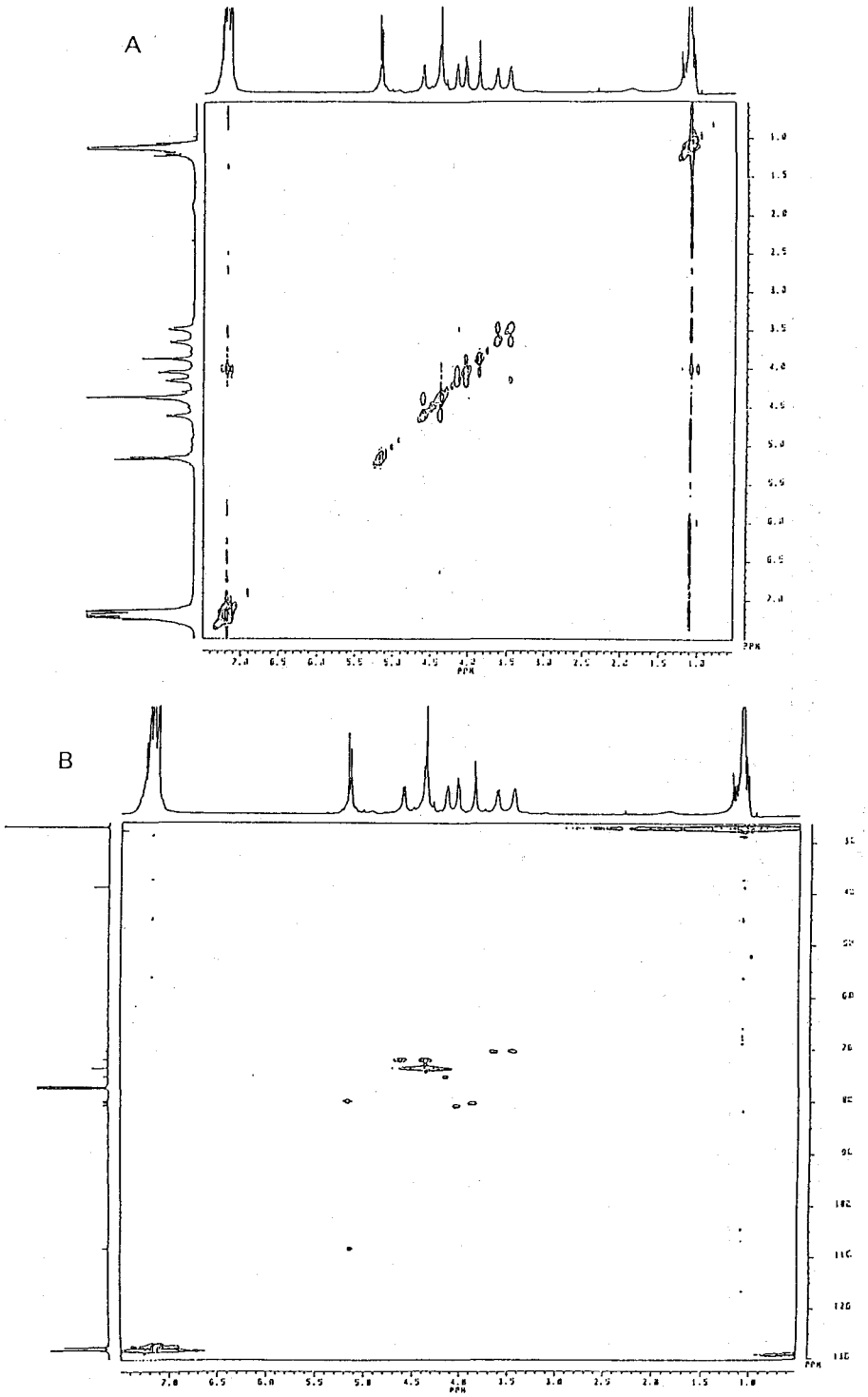


Figure 4. 2D-NMR spectra of 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan (Table 3, experiment no. 31); (A) plot from COSY experiment, and (B) plot from HMQC experiment ($CDCl_3$ as solvent).

Table 4

^{1}H-NMR Chemical Shifts of 3,6-Di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan

	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	Benzyl-H
δ, ppm	5.14	5.17	3.87	4.05	4.15	3.64	3.46	4.61, 4.36, 4.38

Table 5

^{13}C-NMR Chemical Shifts of 3,6-Di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan

	C-1	C-2	C-3	C-4	C-5	C-6	Benzyl-C		C=O
δ, ppm	107.95	79.61	79.95	80.41	74.96	70.09	71.67	73.33	177.13

derivative are known to appear at 100.5 ppm and 95.7 ppm, [29] respectively. The chemical shift of C-1 resonance of the acetylated poly(**2**) is clearly different from that of cellulose acetate. Therefore, it was concluded that the stereoregular poly(**2**) is 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan. This stereoregular polysaccharide derivative has a high degree of crystallinity, and a melting point of *ca.* 120°C determined by microscopic observation.

The ^{1}H resonances for the completely stereoregular poly(**2**)s were assigned *via* their cross-peaks in the COSY spectrum (Figure 4A). The ^{13}C resonances were assigned by comparing the ^{1}H assignments with the ^{1}H-^{13}C correlation data obtained from an HMQC experiment (Figure 4B). The assignments of proton and carbon peaks are summarized in Tables 4 and 5, respectively.

The relationships between the reaction conditions and stereoregularity are shown in Table 3. The stereoregular (1→5)-β-D-glucofuranan derivatives were obtained in four kind of solvents. Phosphorus pentafluoride, boron trifluoride etherate and antimony pentachloride gave stereoregular poly(**2**)s at -30 °C. Trifluoromethanesulfonic anhydride did not cause stereoregular polymerization at -30 °C, as in the case of polymerization of **1**. Stereoregularities of poly(**2**)s increase with a decrease of concentration of PF_5 catalyst (Table 3, experiment nos. 21, 22, and 23).

The fact that polymerization of **2** produced a stereoregular β-D-glucofuranan derivative indicates that the neighboring participation of 2-*O*-pivaloyl groups strongly affects the polymerization of **2** to yield stereoregular poly(**2**)s.

2.1.3 Determination of structure of poly(3)s synthesized from 3

^{13}C-NMR spectrum (Figure 5A) of poly(**3**) (Table 6, experiment no. 15) shows a single anomeric peak at 106.8 ppm, indicating a stereoregular poly(**3**). Taking into account the fact that D-glucans with high negative specific rotation generally have β-configuration, the poly(**3**) having $[\alpha]_D$ -59.3° is thought to be a stereoregular (1→5)-β-D-glucofuranan derivative or a stereoregular (1→4)-β-D-glucopyranan derivative. On the other hand, it is known that the C-1 peak of the cellotetraose derivative with the

Table 6. Polymerizations of 1,4-Anhydro-α-D-glucopyranose Derivatives[a]

exp. no.	monomer	initiator	temp, °C	time h	yield, %	$[\alpha]_D$, deg	10^{-3} M_{GPC}[e]	$\overline{DP_n}$
1	**1**	PF_5	-30	25	65[b]	+79.7	10.4	**24.3**
2	**1**	$BF_3 \cdot Et_2O$	-30	21	66[b]	+72.9	8.0	18.9
3	**1**	$SbCl_5$	-30	20	80[b]	+43.4	1.9	4.3
4	**1**	PF_5	0	20	82[b]	+88.9	9.3	21.8
5	**1**	PF_5	20	17	11[b]	+68.1	2.7	6.4
6	**1**	$BF_3 \cdot Et_2O$	20	20	56[b]	+58.1	5.1	12.1
7	**1**	$SbCl_5$	20	16	62[b]	+27.2	3.1	7.3
8	**2**	PF_5	-30	34	87[b]	-66.9	9.4	**22.0**[f]
9	**2**	$BF_3 \cdot Et_2O$	-30	60	78[b]	-69.3	7.5	17.6[f]
10	**2**	$SbCl_5$	-30	20	100[c]	-65.6	3.4	8.1[f]
11	**2**	PF_5	20	15	74[b]	-5.8	1.4	3.3
12	**2**	$BF_3 \cdot Et_2O$	20	20	86[b]	-19.0	4.7	11.0
13	**2**	$SbCl_5$	20	1	*ca.* 100[c]	-23.4	2.2	5.2[e]
14	**3**	PF_5	-30	239	trace	---	---	---
15	**3**	$BF_3 \cdot Et_2O$	-30	136	42[b]	-59.3	10.0	**23.4**[f]
16	**3**	$SbCl_5$	-30	20	100[c]	-57.9	6.3	14.9[f]
17	**3**	PF_5	20	240	trace	---	---	---
18	**3**	$BF_3 \cdot Et_2O$	20	18	100[c]	-15.7	3.2	7.6
19	**3**	$SbCl_5$	20	1.5	100[c]	-48.0	4.6	11.0[f]
20	**4**	PF_5	-30	26	trace	---	---	---
21	**4**	$BF_3 \cdot Et_2O$	-30	17	7[d]	---	1.4	3.3
22	**4**	$SbCl_5$	-30	17	7[d]	---	2.0	4.8
23	**4**	PF_5	20	24	35[d]	---	1.9	4.4
24	**4**	$BF_3 \cdot Et_2O$	20	16	*ca.* 100[c]	-26.0	2.5	**6.2**
25	**4**	$SbCl_5$	20	16	7[d]	---	1.6	3.7

[a] Initiator concentration: 5 mol %; solvent: CH_2Cl_2: monomer / solv. 50 g/100mL. [b] Polymer was imsoluble fraction in *n*-hexane. [c] No unreacted monomer was detected. [d] Polymer was separated from unreacted monomer by PTLC (EtOAc/*n*-hexane, v/v, 1:4). [e] Number-averaged molecular weight of polysaccharide was determined by gel permeation chromatography (GPC) using polystyrene standards. [f] Stereoregular (1→5)-β-D-glucofuranan derivative was given.

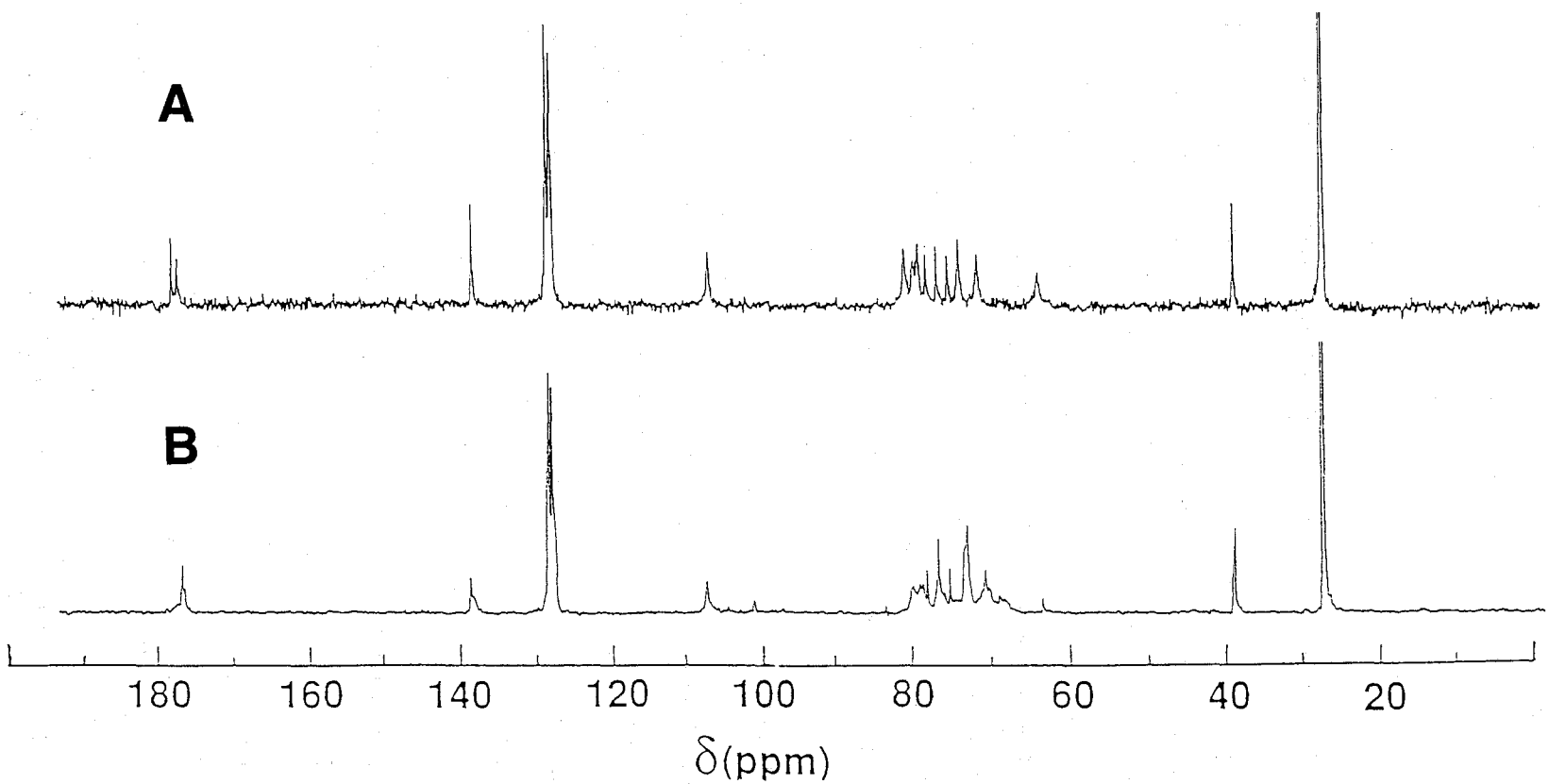


Figure 5. ^{13}C-NMR spectra of (A) poly(**3**) prepared by BF_3Et_2O at -30 °C (Table 6, experiment no. 15), (B) poly(**4**) prepared by BF_3Et_2O at 20 °C (Table 6, experiment no. 24) ($CDCl_3$ as solvent).

same protective group system (benzyl group at the 3-*O* position, and pivaloyl groups at the 2-*O* and 6-*O* positions) appears at 100.0 ppm. [17] Therefore, it was concluded that the stereoregular poly(**3**) is a 3-*O*-benzyl-2,6-di-*O*-pivaloyl-(1→5)-β-D-glucofuranan.

2.1.4 Determination of structure of poly(4)s synthesized from 4

According to the same strategy as described above, ^{13}C-NMR spectrum (Figure 5B) of poly(**4**) having $[\alpha]_D$ -26.0° (Table 6, experiment no. 24) shows two anomeric peaks consisting of 107.5 (main) and 101.4 ppm (minor). In order to assign these peaks, the poly(**4**) was converted into its acetyl derivative. The anomeric peaks of acetylated poly(**4**) appeared at 106.3 (main) and 101.2 ppm (minor). Anomeric peaks of acetylated (1→4)-α-P, (1→5)-α-F, (1→4)-β-P, and (1→5)-β-F units are known to appear at 95.7, 100.4, 100.5, and 106.2 ppm, respectively. [25] Therefore the main anomeric peak at 107.5 ppm of the poly(**4**) was assigned to (1→5)-β-F units, and a minor anomeric peak of the poly(**4**) at 101.2 ppm may indicate the presence of (1→5)-α-F or (1→4)-β-P units.

2.2 Substituent effects on ring-opening polymerization of 1,4-anhydro-α-D-glucopyranose derivatives

An influence of a substituent group at C_2-position makes a difference in a structure of polysaccharide (Section **2.2.3**). Due to an substituent effect of 3-*O*-benzyl group, a stereoregular polysaccharide is produced (Sections **2.2.3**, and **2.2.4**).

2.2.1 Molecular weights of poly(1)s and poly(2)s synthesized from 1 and 2, respectively

The influence of reaction conditions on the molecular weight of the polymers was investigated. The results are summarized in Tables 2 and 3. Number-average molecular weights of poly(**1**)s and poly(**2**)s, determined by gel permeation chromatography (GPC) using polystyrene standards, ranged from 4000 ($\overline{DP_n}$ = 9.5) to 12500 ($\overline{DP_n}$ = 29.3), and 3400 ($\overline{DP_n}$ = 8.1) to 18100 ($\overline{DP_n}$ = 42.6), respectively.

Compound **1** polymerized at -78 °C, but compound **2** did not at that temperature because **2** crystallized out at -78 °C. Number-average molecular weights of poly(**2**)s obtained using phosphorus pentafluoride as catalyst at -30°C decreased in the order: in toluene > dichloromethane > nitromethane > 1,2-dichloroethane (Table 3, experiment nos. 23, 31, 36, and 37), while, especially in dichloromethane, decreased with decrease in concentration of the compound **2** (monomer/solvent (g/mL), 50, 33, and 25) (Table 3, experiment nos. 23, 24, and 25), and with an increase of concentration of phosphorus pentafluoride (5, 10, and 15 mol %) (Table 3, experiment nos. 21, 22, and 23). Compound **2** polymerized more readily than **1** in toluene (see experiment nos. 12 and 31).

2.2.2 Substituent effect on molecular weight of polysaccharides

Molecular weights of poly(**1**)s, poly(**2**)s, and poly(**3**)s decrease with an increase of reaction temperature, but those of poly(**4**)s are low under all conditions undertaken. The polymerizability of four monomers is in the order of **1** ≅ **2** ≅ **3** >> **4**, as judged from the highest molecular weight obtained from these monomers (Table 6, experiment nos. 1, 8, 15, and 24) and from the yield of polymer at -30 °C.

Generally, the electron-donating benzyl group accelerates reactivity, but the electron-withdrawing acetyl group retards both the glycosylations and polymerizations of anhydro-sugars. For example, Zachoval *et al.* [32] reported that 1,6-anhydro-β-D-glucopyranose triacetate was less reactive than 1,6-anhydro-β-D-glucopyranose tribenzylether.

Monomers **1** and **2** having two benzyl groups expectedly afforded polymer with high molecular weight, and monomer **4** having one benzyl group did not afford polymer under various reaction conditions (Table 6, experiment nos. 20-25), but unexpectedly monomer **3** having only one benzyl group afforded polymer with high molecular weight. Consequently, the present results indicate that the important factor for accelerating polymerizability is not only the number of the substituent benzyl groups but also the positions where benzyl groups are attached. The common substituent among monomers **1**, **2**, and **3** is a benzyl group at the 3-*O* position: monomer **4** does not have

a benzyl group at 3-*O* position. Thus, the benzyl group at the 3-*O* position is indispensable for yielding glucan with high molecular weight.

Comparing monomers **2** having a benzyl group at the 6-*O* position and **3** having a pivaloyl group at the 6-*O* position, there is little difference in molecular weight under optimum reaction conditions (Table 6, experiment nos. 8 and 15). Consequently, the benzyl group at the 6-*O* position did not have much effect on polymerizability.

2.2.3 Substituent effect on stereoregularity of polysaccharides

Substituent groups at O-2 greatly affect specific rotation, as shown in Table 6. All poly(**1**)s are dextrorotatory. The polymerization of **1** having a benzyl group at the 2-*O* position gave a non-stereoregular polymer mainly consisting of (1→5)-α-F units. On the other hand, all poly(**2**)s, poly(**3**)s, and poly(**4**)s are levorotatory. All these monomers have a pivaloyl group at the 2-*O* position. The polymerization of **2** gave a stereoregular (1→5)-β-D-glucofuranan derivative (Table 6, experiment nos. 8-10, and 13). [28] Polymerization of **3** also gave a stereoregular (1→5)-β-D-glucofuranan derivative (Table 6, experiment nos., 15, 16, and 19). Polymerization of **4** tended to give (1→5)-β-F units, but none of conditions afforded a stereoregular poly(**4**), although monomer **4** has the same 2-*O*-pivaloyl group as monomers **2** and **3** have (Table 6, experiment nos. 20 - 25). Consequently, it turned out that the benzyl group at the 3-*O* position is indispensable for obtaining a stereoregular polysaccharide.

The reason of the indispensability is hereinafter described. It is predicted that the favorable complexation of Lewis acids with both a C_5- and a C_3-oxygen tends to occur to result in enhancement of polymerizability and stereoregularity, because the electron-donating 3-*O*-benzyl group raises the electron density of the C_3-oxygen and consequently elevates the coordination power with Lewis acids. The electron-withdrawing pivaloyl group at 3-*O* position, on the contrary, weakens the coordination power of the Lewis acids so that polymerizability and stereoregularity are lowered.

The fact that both polymerization of **2** having a benzyl group at the 6-*O* position and that of **3** having pivaloyl group at 6-*O* position gave stereoregular (1→5)-β-D-

glucofuranan derivatives with almost the same $\overline{DP_n}$ under these optimum conditions (Table 6, experiment nos. 8 and 15) indicates that the substituent group at the 6-*O* position hardly affects either stereoregularity or polymerizability.

2.2.4 Importance of 3-*O*-benzyl group of 1,4-anhydro-α-D-glucopyranose derivative on ring-opening polymerization

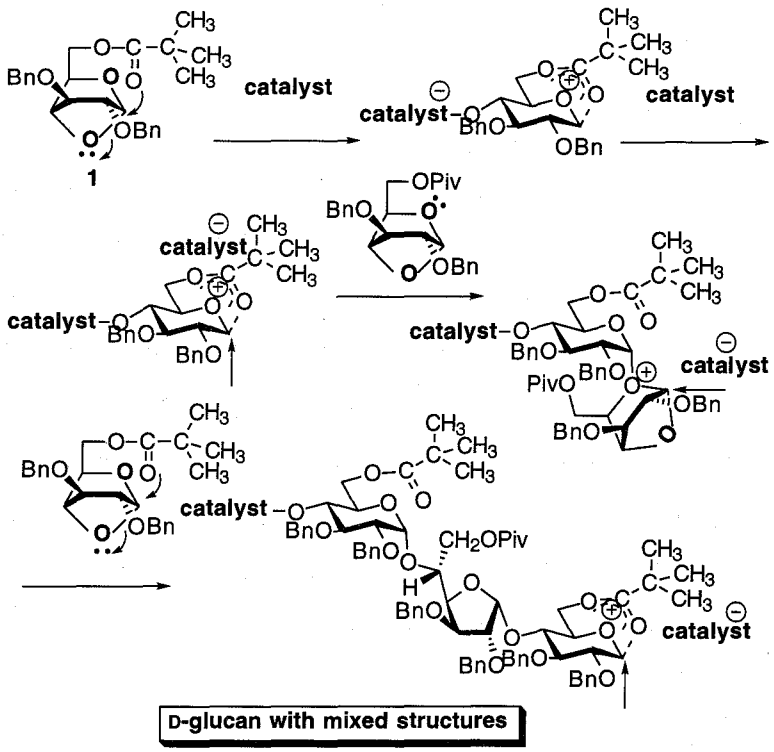
Substituent groups at the 6-*O* position did not remarkably affect stereoregularity or polymerizability, comparing results from monomers **3** and **2**. It was confirmed that the benzyl group at the 3-*O* position has a special function for yielding a stereoregular polysaccharide with high molecular weight in a ring-opening polymerization (results from monomers **4** and **2**). It was reconfirmed that the presence of the pivaloyl group at the 2-*O* position makes the polysaccharide take the β-configuration (results from monomers **3** and **1**). Polysaccharides with high molecular weight tend to have high stereoregularity as shown in Table 6 (experiment nos. 8, 9, 15, and 16). Consequently, both the pivaloyl group at the 2-*O* position and the benzyl group at the 3-*O* position are indispensable for yielding stereoregular (1→5)-β-D-glucofuranan derivatives with high molecular weight.

Furthermore, polymerization of 1,4-anhydro-α-D-glucopyranose was found to always preferentially afford (1→5)-D-glucofuranose units, not (1→4)-β-D-glucopyranose units. These results agreed with the cases of the ring-opening polymerization of 2,7-dioxabicyclo-[2.2.1]heptane [33] and that of 1,4-anhydro-2,3,6-tri-*O*-benzyl-α-D-glucopyranose [14]. Thus, it is also concluded that 1,4-anhydro-α-D-glucopyranose skeleton is not suitable for yielding a (1→4)-β-D-glucopyranan, that is, cellulose molecule.

2.2.5 Mechanism of polymerization

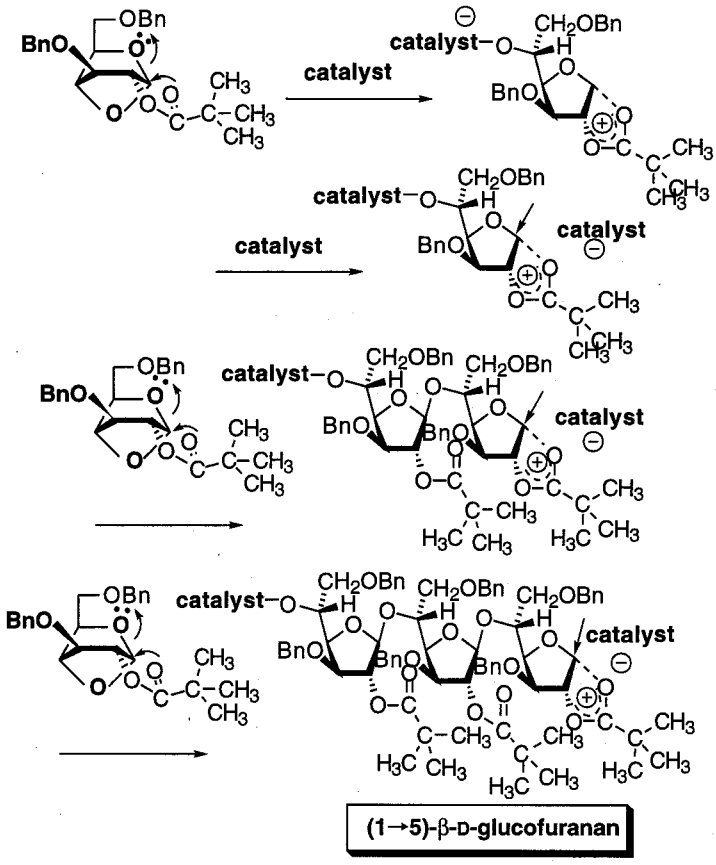
Scheme 6 illustrates the proposed propagation mechanism of polymerization of **1** to produce (1→4)-α-P units. Phosphorus pentafluoride as catalyst (initiator) coordinates with the acetal oxygen of the 1,4-anhydro ring, the carbonyl oxygen of the pivaloyl group at 6-*O* attacks C-1 from the β-side to form a dioxacarbenium-ion

intermediate, and the oxygen of the anhydro ring of the next monomer attacks from the opposite side, *i. e.*, α-side, of the intermediate to form (1→4)-α-P units. Without such neighboring group participation of the 6-*O*-acyl group, the (1→5)-α-F units are produced as expected from the results of Uryu *et al.*. [14]



Scheme 6

Scheme 7 illustrates the proposed propagation mechanism of the polymerization of **2** to yield (1→5)-β-D-glucofuranan. The production of (1→5)-β-F units clearly indicates neighboring group participation of the pivaloyl group at the 2-*O* position. The catalyst coordinates with the oxygen of the 1,5-anhydro ring, the electron density of which increases due to the electron-donating benzyl group at the 6-*O* position. This coordination would result in the formation of (1→5)-β-furanose ring. The carbonyl oxygen of the pivaloyl group at the 2-*O* position attacks C-1 from the α-side to form a dioxacarbenium-ion intermediate, and then the oxygen of the 1,5-anhydro ring of next monomer attacks from the opposite side, *i. e.*, β-side, of the intermediate to form (1→5)-β-F sequences.



Scheme 7

2.3 Deprotection of substituted polymers

Stereoregular 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan (poly(**2**)s) was debenzylated and depivaloylated with sodium in liquid ammonia to give free (1→5)-β-D-glucofuranan, as shown in Scheme 8. The IR spectrum of free (1→5)-β-D-glucofuranan was compared with that of the (1→5)-β-D-glucofuranan derivative, as shown in Figure 6. In spectrum (Figure 6A) of the (1→5)-β-D-glucofuranan derivative, there are bands due to the pivaloyl group at 1740 cm^{-1} and due to benzyl groups at 700 and 740 cm^{-1}. In spectrum (Figure 6B) of free (1→5)-β-D-glucofuranan, those bands cannot be found. The ^{13}C-NMR spectrum of free (1→5)-β-D-glucofuranan (poly(**2**)') in D_2O is shown in Figure 7 (DSS (sodium 2,2-dimethyl-2-silapentane-5-sulfonate) as an external standard). Signals from the protective groups have completely disappeared. The signal of the anomeric peak appears at 108.0 ppm.

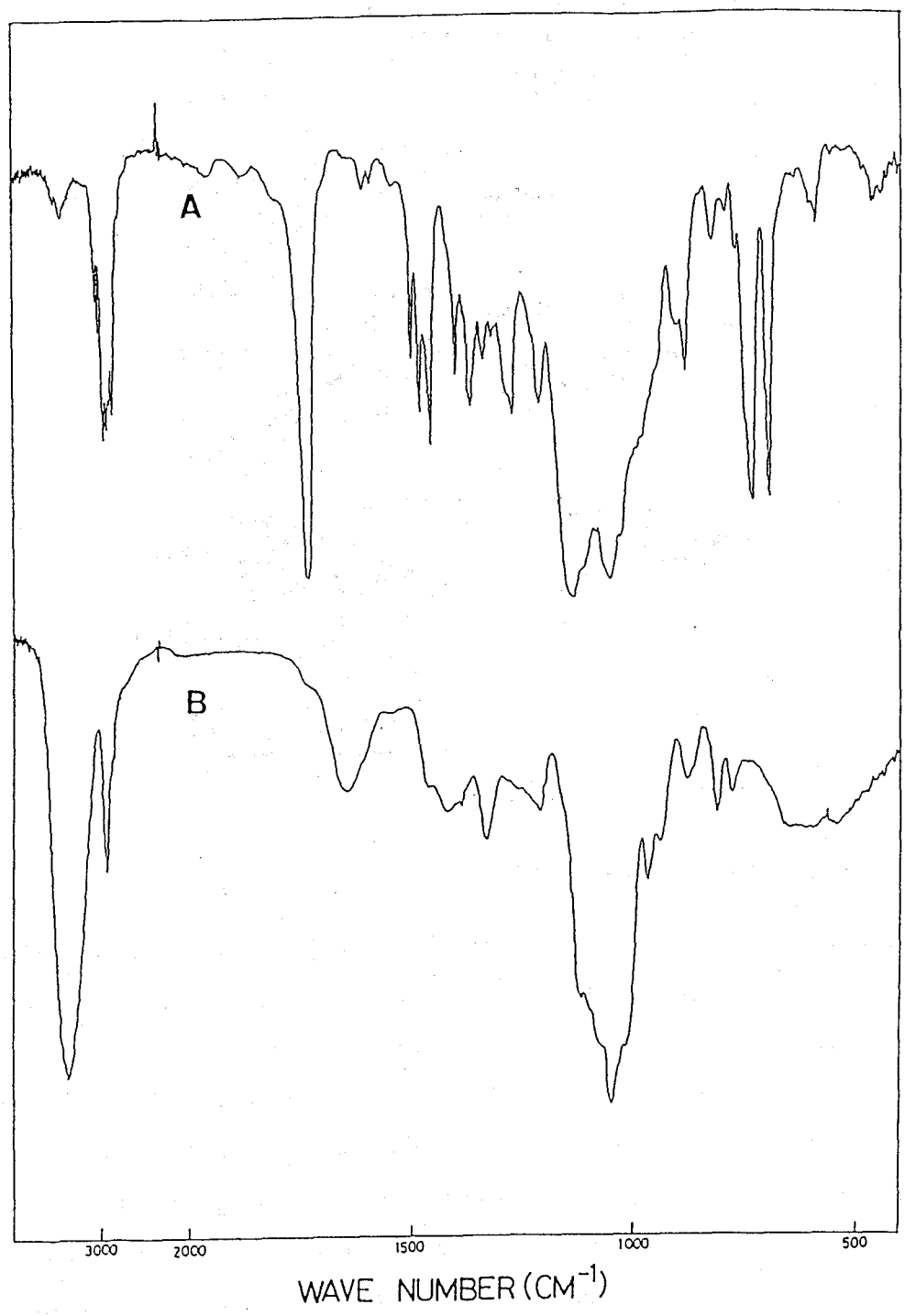


Figure 6. IR spectra of (A) 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan, and (B) deprotected (1→5)-β-D-glucofuranan.

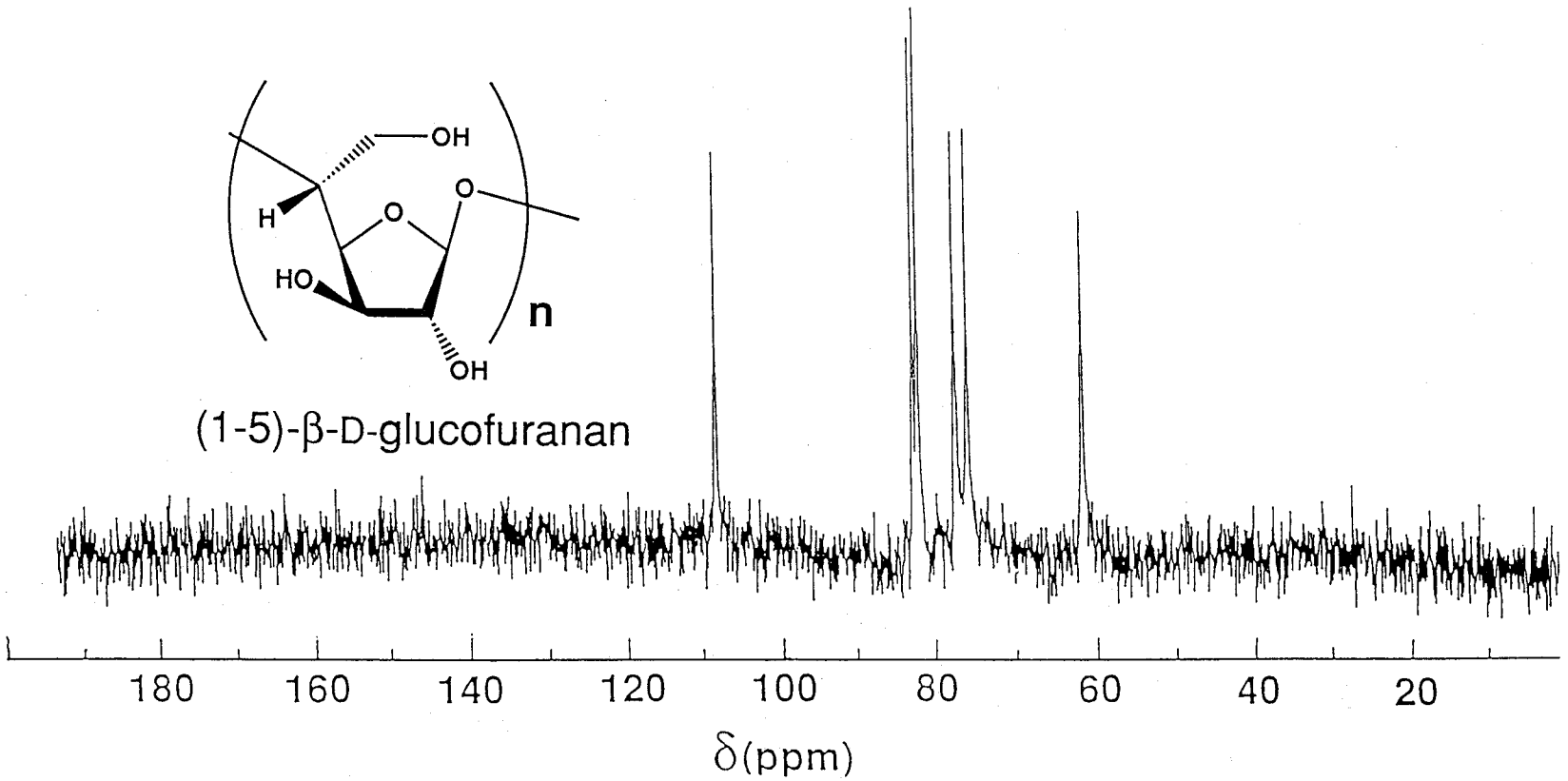
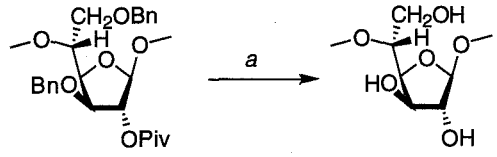


Figure 7. ^{13}C-NMR spectrum of (1→5)-β-D-glucofuranan (in D_2O, DSS as an external standard).



[a] Na metal / liq. NH_3 / toluene / 1,2-dimethoxyethane / -78°C

Scheme 8. Deprotection of 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranans

2.4 Summary

To investigate the substituent effects at the 2-*O*, 6-*O*, and 3-*O* positions on ring-opening polymerization, 1,4-anhydro-2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose (**1**) 1,4-anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (**2**) [24], 1,4-anhydro-3-*O*-benzyl-2,6-di-*O*-pivaloyl-α-D-glucopyranose (**3**), and 1,4-anhydro-6-*O*-benzyl-2,3-di-*O*-pivaloyl-α-D-glucopyranose (**4**) [25] were selected as starting monomers and were polymerized under various reaction conditions: initiator-, solvent-, monomer concentration- and temperature-dependence.

Polymerization of **1** gave non-stereoregular polymers consisting of mainly (1→5)-α-D-glucofuranosidic units with $[\alpha]_D$ value of *ca.* +84°. Polymerization of **2** with phosphorus pentafluoride catalyst produced new stereoregular polysaccharide derivatives, 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranans ($\overline{DP_n}$ = 42.6) with $[\alpha]_D$ value of ca. -66°. Polymerization of **3** also produced (1→5)-β-D-glucofuranan derivative. Polymerization of **4**, however, gave non-stereoregular polysaccharides consisting mainly of (1→5)-β-D-glucofuranosidic units. Substituted polymers were characterized by ^1H- and ^{13}C-NMR spectroscopy, polarimetry, and gel permeation chromatography.

Finally, it was concluded that both the pivaloyl group at the 2-*O* position and the benzyl group at the 3-*O* position are indispensable for yielding stereoregular (1→5)-β-D-glucofuranan derivatives with high molecular weight, and that a substituent group at the 6-*O* position hardly affects stereoregularity or polymerizability. The 1,4-anhydro-α-D-glucopyranose skeleton is not suitable for yielding a (1→4)-β-D-glucopyranan, *i.e.*, cellulose.

Furthermore, debenzylation and depivaloylation of the substituted polymers afforded unsubstituted (1→5)-β-D-glucofuranan. The electronic effect on the ring-opening polymerization and mechanism of the ring-opening polymerization were discussed (Section **2.2.5**). After all, the author has for the first time succeeded in the synthesis of the (1→5)-β-D-glucofuranan with $[\alpha]_D$ value of ca. -204°.

CHAPTER 3

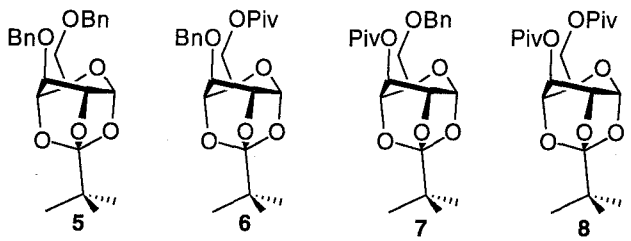
Selection and Synthesis of α-D-Glucopyranose 1,2,4-Orthopivalate Derivatives: Starting Materials for Ring-Opening Polymerization

Introduction

In chapter 2, polymerization of 1,4-anhydro-α-D-glucopyranose was always found to preferentially afford (1→5)-D-glucofuranose units, not (1→4)-β-D-glucopyranose units. Thus, it was concluded that 1,4-anhydro-α-D-glucopyranose skeleton was not suitable for yielding a (1→4)-β-D-glucopyranan, that is, cellulose molecule.

One strategy for realizing the highly regioselective 1,4-scission is to substitute 1,4-ether bond of 1,4-anhydro-α-D-glucopyranose derivatives for another more reactive linkage such as that of orthoester derivative. Several cationic ring-opening polymerizations of such tricyclic intramolecular orthoesters prepared from arabinose and xylose have been studied extensively by Bochkov, Kochetkov, and their co-workers [34]: they neither considered the substituent effect on polymerization, nor achieved a stereoregular polymer.

Finally, the author selected regioselectively acylated tricyclic orthoester derivatives, 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**5**), 3-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**6**), 6-*O*-benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**7**), and 3,6-di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**8**) as a starting monomer for cationic ring-opening polymerization. Substituent effect on ring-opening polymerization of α-D-glucopyranose orthopivalate derivative is described in detail in Chapter 4.



5 **6** **7** **8**

A synthetic method for α-D-glucopyranose 1,2,4-orthoacetate has been found by a previous investigation of Bochkov *et al.*. [35] 1-Halogenized D-glucopyranose peracetate was converted to 1,2-methylorthoacetyl-3,4,6-tri-*O*-acetyl-α-D-glucopyranose, then deacetylated, orthoesterificated to give an α-D-glucopyranose 1,2,4-orthoacetate, finally, acetylated to give a 3,6-di-*O*-acetyl-α-D-glucopyranose 1,2,4-orthoacetate.

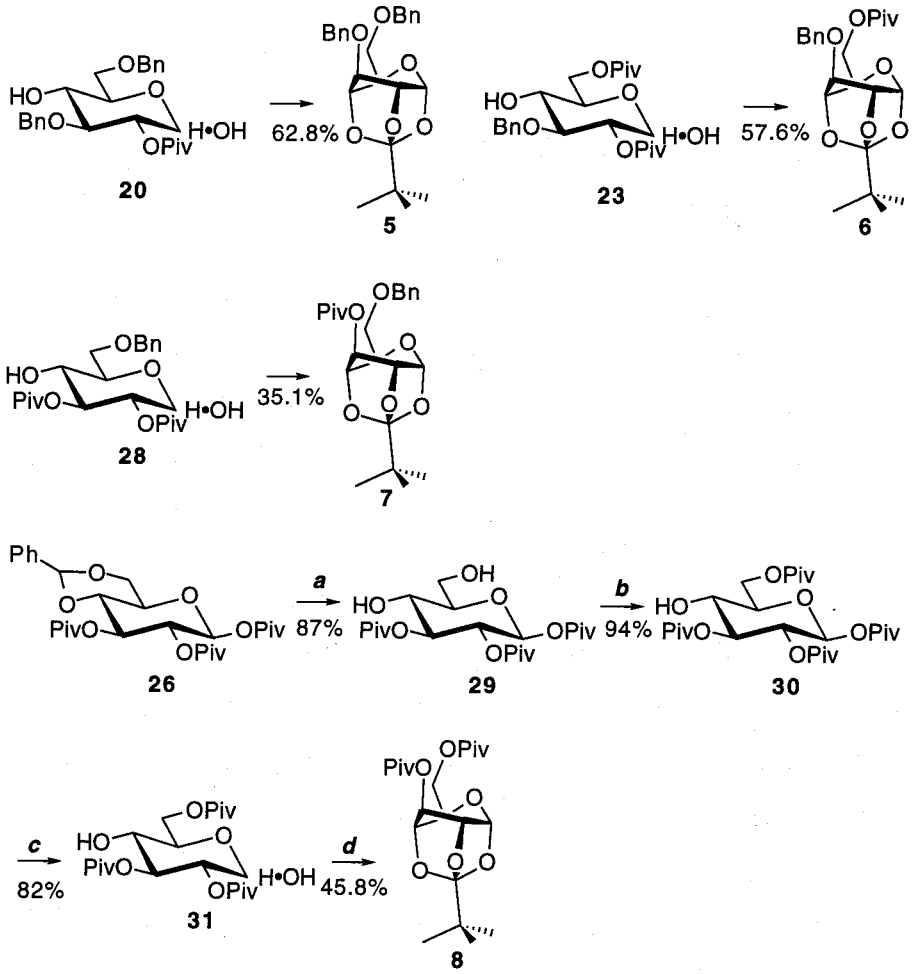
However, the above mentioned synthetic method applied for glucose [35] and xylose [36], particularly final step in the synthetic route, may not be applied to the syntheses of **6** and **7** because selective protection of C_3- or C_6- positions would be difficult.

In this chapter, new synthetic methods for orthoester derivatives are described. Orthoesterification using *N,N'*-carbonyldiimidazole at the final step was carried out under a mild condition so that all protective groups are stable at that step. In addition, the new procedure could be widely applicable in the synthesis of a series of orthoester derivatives.

3.1 Syntheses of 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (5), 3-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (6), 6-*O*-benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (7), and 3,6-di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (8).

In a synthetic route for compound **5**, compound **20** was also obtained through the synthetic method for yielding the anhydro sugar derivative **2**. Compound **20** [23] was refluxed with an equimolar amount of *N, N'*-carbonyldiimidazole in benzene to afford orthoester derivative **5** in about 60% yield. The structure of **5** was confirmed by elemental analysis and spectral analyses: IR (no carbonyl peak at 1740 cm^{-1}), ^{1}H-NMR (C_1-H: δ 5,79, d, J = 4.86), ^{13}C-NMR (no carbonyl peak and orthoester quaternary carbon at δ 123.10). The reagent, *N, N'*-carbonyldiimidazole, has been used as the dehydrating reagent for the preparation of lactones, [37] peptides, [38] glucosides, [39] and cyclic carbonates [40] from diol compounds. [41] The reagent

preferentially attacks an hydroxyl group that is more acidic than 4-OH of compound **20** to give a 1-*O*-carbonylimidazole derivative, which is further converted to a dioxocarbenium ion intermediate with removal of the carbonylimidazole group and then to orthoester **5** by intramolecular attack of 4-OH. After all, the orthoester derivative **5** was obtained from D-glucose in 8 reaction steps.



[a] p-TsOH / MeOH / r.t. / 2h, [b] PivCl / pyridine / r.t. / 1h, [c] $NH_2NH_2 \cdot H_2O$ / THF / r.t. / 8h, [d] *N,N'*-carbonyldiimidazole / benzene / reflux / 9 days

Scheme 9. Syntheses of orthoester derivatives.

3-*O*-Benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**6**), was prepared from **23** in a 57.6% yield by the same method as described above. In a synthetic route for compound **6**, compound **23** was also obtained through the synthetic method for

yielding the anhydro sugar derivative **3**. The orthoester derivative **6** was obtained from D-glucose in 9 reaction steps.

6-*O*-Benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**7**) was prepared from **28** in a 35.1% yield by the same method as described above. In a synthetic route for compound **7**, compound **28** was also obtained through the synthetic method for giving the anhydro sugar derivative **4**. The orthoester derivative **7** was obtained from D-glucose in 5 reaction steps.

3,6-Di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**8**) was prepared from **31** in a 45.8% yield by the same method as described above. Compound **26** was the same synthetic intermediate as used in the synthesis of compound **7**. Debenzylation of **26** afforded 1,2,3-tri-*O*-pivaloyl-β-D-glucopyranose (**29**) in a 87% yield. Selective 6-*O*-pivaloylation of **29** gave 1,2,3,6-tetra-*O*-pivaloyl-β-D-glucopyranose (**30**) in a 94% yield. Selective 1-*O*-depivalylation of **30** was achieved with hydrazine hydrate to give 2,3,6-tri-*O*-pivaloyl-D-glucopyranose (**31**) in a 82% yield. After all, compound **8** was obtained from D-glucose in 6 reaction steps.

Consequently, compounds **5**, **6**, **7**, and **8** were selected as starting monomers in order to systematically study the effect of acyl groups on ring-opening polymerization of α-D-glucopyranose 1,2,4-orthopivalate derivatives (Scheme 9).

3.2 ^{1}H-NMR Chemical shifts of α-D-glucopyranose 1,2,4-orthopivalate derivatives.

The assignments of proton peaks are summarized in Table 7. C_4-Proton resonances of 3-*O*-pivaloyl derivatives **7** and **8** are shifted to a low magnetic field (δ 5.08 and 5.12 ppm, respectively) comparing with those of 3-*O*-benzyl derivatives **5** and **6** (δ 3.95 and 3.95 ppm, respectively), although C_3-proton resonances of the 3-*O*-pivaloyl derivatives are little shifted. The reason of these chemical shifts is obscure. It is, however, predicted that, owing to 3-*O*-pivaloyl group, electron density of C_4-oxygen of 3-*O*-pivaloyl derivatives **7** and **8** is lower than that of 3-*O*-benzyl derivatives **5** and

Table 7. ^{1}H-NMR Chemical Shifts of α-D-Glucopyranose 1,2,4-Orthopivalate Derivatives

carbon no.	1	2	3	4	5	6		R_2	R_3	R_6
5	5.79	4.42	4.31	3.95	4.60	3.83	3.75	Piv	Bn	Bn
6	5.76	4.39-4.43	4.16	3.95	4.45-4.52	4.31-4.41		Piv	Bn	Piv
7	5.73	4.38	4.31	5.08	4.62	3.61	3.72	Piv	Piv	Bn
8	5.75	4.43	4.25	5.12	4.56	4.38	4.21	Piv	Piv	Piv

6. A relationship between ^{1}H-NMR chemical shifts described above and structure of polysaccharides yielded is mentioned in Chapter 4.

3.3 Summary

In this Chapter, synthetic methods of four new α-D-glucopyranose 1,2,4-orthopivalate derivatives were described. Monomers **5**, **6**, **7** and **8** were synthesized from D-glucose in 8, 9, 5, and 6 reaction steps, respectively.

Characteristics of the present new method for the synthesis of orthoester exist in a final step. [35, 36] That is, substituent group at C_3- and C_6-position has already been introduced before a final step. Orthoesterification using *N,N'*-carbonyldiimidazole at the final step was carried out under a mild condition so that all protective groups were stable at that step. In addition, the new procedure could be widely applicable in the synthesis of a series of orthoester derivatives.

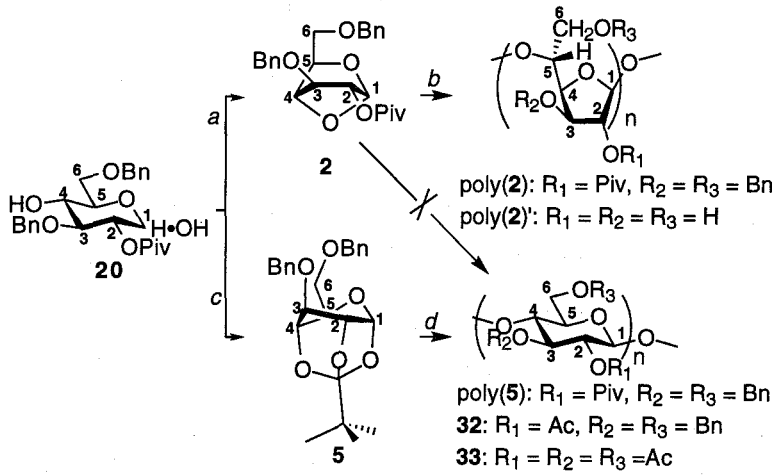
In the case of a previous method of Bochkov *et al.* [35], the rest free hydroxy groups are protected after a formation of orthoester linkage. The method may not be applied directly to the syntheses of **6** and **7** because of limitation of the selective protection between C_3- and C_6-hydroxy groups. For example, in a case of a synthesis of **6**, a regioselective 6-*O*-pivaloylation may be done because primary C_6-hydroxy group is more reactive than secondary C_3-hydroxy one, but subsequent 3-*O*-benzylation would be difficult because a pivaloyl group was unstable under a basic condition of a usual benzylation: the benzylation should be done under an acidic conditions, but under which the orthoester linkage may be unstable.

An advantage of the previous method is to be a short synthetic route: if an α-D-glucopyranose 1,2,4-orthopivalate were synthesized according to the previous method, monomer **5** would be obtained from D-glucose in 6 reaction steps. However, reaction steps for yielding other monomers **6**, **7** and **8** would not change so much if they were synthesized according to the previous method.

Taking into account total advantage, the present new method is more valuable than the previous procedure.

CHAPTER 4

Ring-opening polymerization of α-D-glucopyranose 1,2,4-orthopivalate derivatives



[a] p-TsOH / benzene/ reflux / 55%, [b] PF_5 / toluene / -30°C,

[c] *N,N'*-carbonyldiimidazole / benzene/ reflux, 62.8%, [d] Ph_3CBF_4 / CH_2Cl_2 / r.t.

Introduction

As described in the previous chapter, the author recently succeeded in the first synthesis of the stereoregular polysaccharide, 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranan poly(**2**) from 1,4-anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (**2**) with the same protective system as compound (**20**) by cationic ring-opening polymerization. Then, the polymer was converted to a non-natural polysaccharide, (1→5)-β-D-glucofuranan poly(**2**)'. [28] Furthermore, 1,4-anhydro-α-D-glucopyranose derivatives were polymerized under various conditions to investigate the substituent effects at 2-*O*, 3-*O*, and 6-*O* positions on the ring-opening polymerization. The author confirmed that the benzyl group at 3-*O* position has a special function for yielding a stereoregular polysaccharide with high molecular weight and that the pivaloyl group at 2-*O* position promotes polysaccharide β-configuration of the glucosidic center. Consequently, both the pivaloyl group at 2-*O* position and the benzyl group at 3-*O* position are indispensable for yielding stereoregular (1→5)-β-D-

glucofuranan derivatives with high molecular weight. [25] Thus, it was demonstrated that substituent effect obtained from the stepwise synthesis of cellooligosaccharides can be also applied to the ring-opening polymerization of anhydro sugars.

For synthesizing cellulose from 1,4-anhydro-α-D-glucopyranose derivatives, however, regiospecific ring-opening, *i. e.*, 1,4-bond scission, giving 1,4-bond formation between repeating anhydro glucopyranose units have to be achieved. All trials for the regiospecific 1,4-ether bond cleavage of 1,4-anhydro-α-D-glucopyranose derivatives were unsuccessful in spite of many experiments carried out under various reaction conditions. [23] Thus, these results finally indicate that the cationic ring-opening polymerization of bicyclic 1,4-anhydro-α-D-glucopyranose derivatives such as compound **2** always afford preferentially (1→5)-D-glucofuranan rather than (1→4)-D-glucopyranan, coinciding with the results from model experiments with 2,7-dioxabicyclo [2.2.1] heptane by Hall *et al.* [33]: that is, it is impossible to synthesize stereoregular (1→4)-β-D-glucopyranan from the bicylic 1,4-anhydro-α-D-glucopyranose derivatives. One strategy for yielding the highly regioselective 1,4-scission is to substitute 1,4-ether bond of 1,4-anhydro-α-D-glucopyranose derivatives for another more reactive linkage such as that of orthoester **5**. Several cationic ring-opening polymerizations of such tricyclic intramolecular orthoesters prepared from arabinose and xylose have been studied extensively by Bochkov, Kochetkov, and their co-workers [34]: they, however, neither considered the substituent effect on polymerization, nor achieved a stereoregular polymer.

In the previous chapter, regioselectively acylated tricyclic orthoester derivatives, 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**5**), 3-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**6**), 6-*O*-benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**7**), and 3,6-di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**8**) as a starting monomer for cationic ring-opening polymerization were selected.

In this chapter, the author describes that cellulose, (1→4)-β-D-glucopyranan was for the first time synthesized by cationic ring-opening polymerizations of **5** and **6** into 3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranan, and 3-*O*-benzyl-2,6-di-*O*-pivaloyl- β-D-

glucopyranan respectively, and subsequent removal of the protective groups. Polymerization of **7** did not afford stereoregular polysaccharide. Substituent effects in the ring-opening polymerizations of orthoester derivatives are discussed. [42, 43]

4.1 Ring-opening polymerization of α-D-glucopyranose 1,2,4-orthopivalate derivatives

4.1.1 Determination of structure of poly(5)s synthesized from 5

Polymers obtained from experiment nos. 1 - 9 in Table 8 gave the same ^{1}H- and ^{13}C-NMR spectra, shown in Figures 8 and 9. The following data are those of the poly(**5**)s from experiment no. 9. The ^{1}H resonances for the poly(**5**)s were assigned *via* their cross-peaks in the H-H COSY spectrum (Figure 10A). The ^{13}C resonances were assigned by comparing the ^{1}H assignments with ^{1}H- ^{13}C correlation data in the C-H COSY spectrum (Figure 10B). The assignments of proton and carbon peaks are summarized in Table 9.

Each ring proton appears clearly even though the substance is a polymer, which indicates high stereoregularity of the poly(**5**)s. This is also supported by the fact that the poly(**5**)s is a crystalline compound with melting point 206 - 217 °C.

The relatively large coupling constant of the ring protons (J = approximately 7 Hz) suggests that the poly(**5**)s consists of glucopyranosyl repeating units with $^{4}C_{1}$-conformation, not of furanosyl units. [44] The presence of the pivaloyl group is supported by various spectral data: IR spectrum (1740 cm^{-1}), ^{1}H-NMR (δ 0.97-1.13 ppm, 9H) and ^{13}C-NMR (δ 27.16, 38.66). This group must exist at a C_2-*O*-position of the repeating glucopyranosyl units, because the C_2-proton appears at the lowest magnetic field (δ 4.95, t, J = 8.7 Hz) among the ring protons. Thus, the above spectroscopic data strongly indicate that the poly(**5**)s have exactly the (1→4)-D-glucopyranan skeleton with $^{4}C_{1}$-conformation, although there is a possibility of producing both (1→2)- and (1→4)-D-glucans on the cationic ring opening polymerization of the 1,2,4-orthoester.

Table 8. Polymerization of 3,6-Di-*O*-benzyl–α-D-glucopyranose 1,2,4-Orthopivalate (**5**)

exp no.	initiator	monomer/solv, g/100mL	temp, °C	time, h	yield, %	$[\alpha]_D$, deg	10^{-3} M_{GPC}	$\overline{DPn}$[d]
1	PF_5	25	-30	63	56[a]	-15.1	3.1	7.2
2	$BF_3 \bullet Et_2O$	25	-30	43	100[b]	-32.8	4.5	10.6
3	Ph_3CSbCl_6	50	-30	151	90[a]	-31.4	3.0	7.0
4	Ph_3CSbCl_6	50	0	78	85[a]	-12.2	1.6	3.7
5	Ph_3CSbCl_6	50	20	14	55[a]	-12.4	1.4	3.3
6	Ph_3CBF_4	50	-30	16	50[a]	-20.1	2.9	6.9
7	Ph_3CBF_4	50	0	18	96[a]	-32.9	3.8	8.9
8	Ph_3CBF_4	50	20	14	93[a]	-35.2	4.5	10.5
9	Ph_3CBF_4	100	20	2	62[c]	-37.2	8.3	19.3

a) Polymer was insoluble fraction in *n*-hexane.
b) No unreacted monomer was detected.
c) Polymer was insoluble fraction in chloroform / *n*-hexane (*ca.* 1 / 5, v / v).
d) Molecular weight was calculated from polystylene standard.

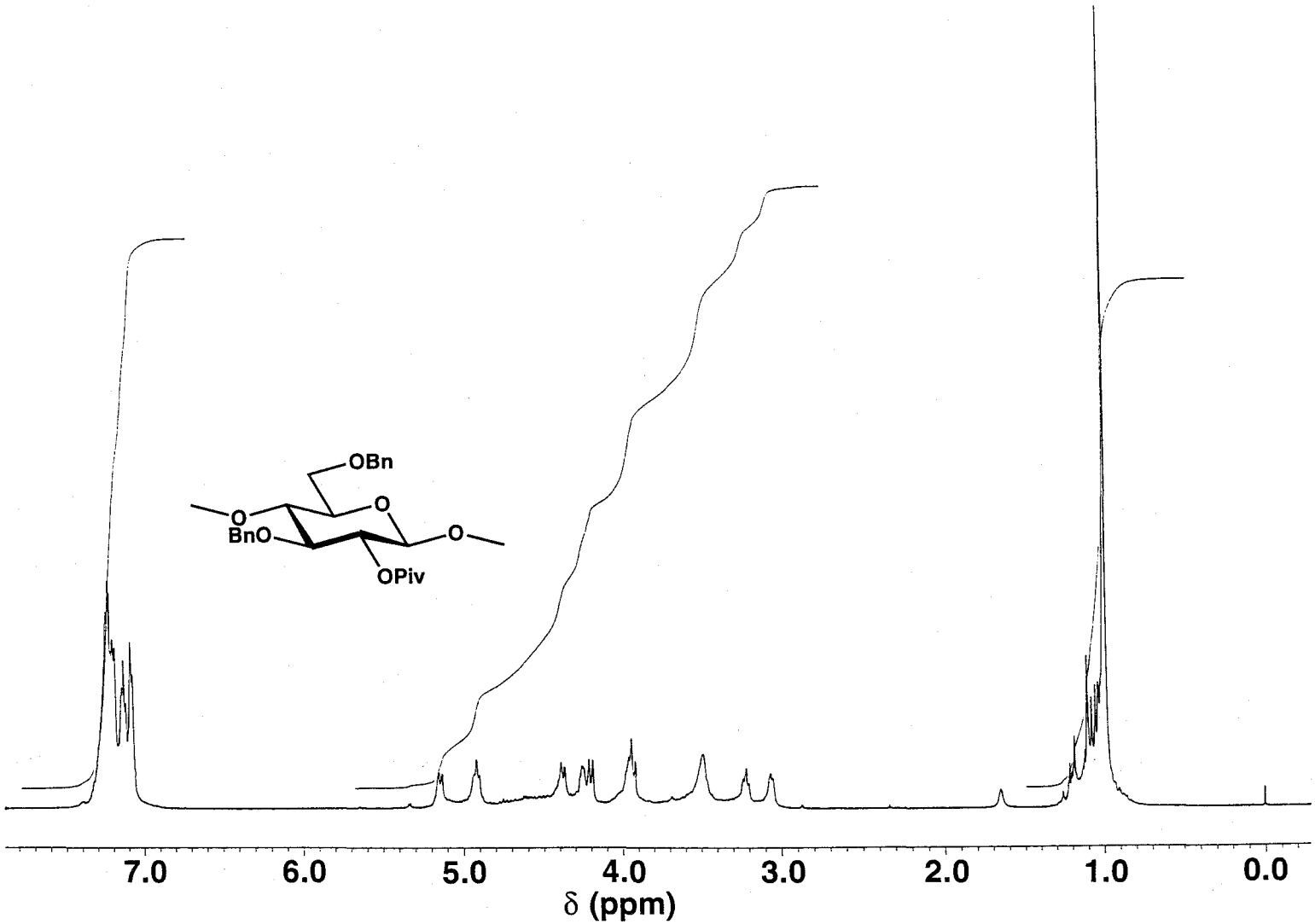


Figure 8. 500-MHz ^{1}H-NMR spectrum of 3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranan poly(**5**) ($CDCl_3$ as solvent).

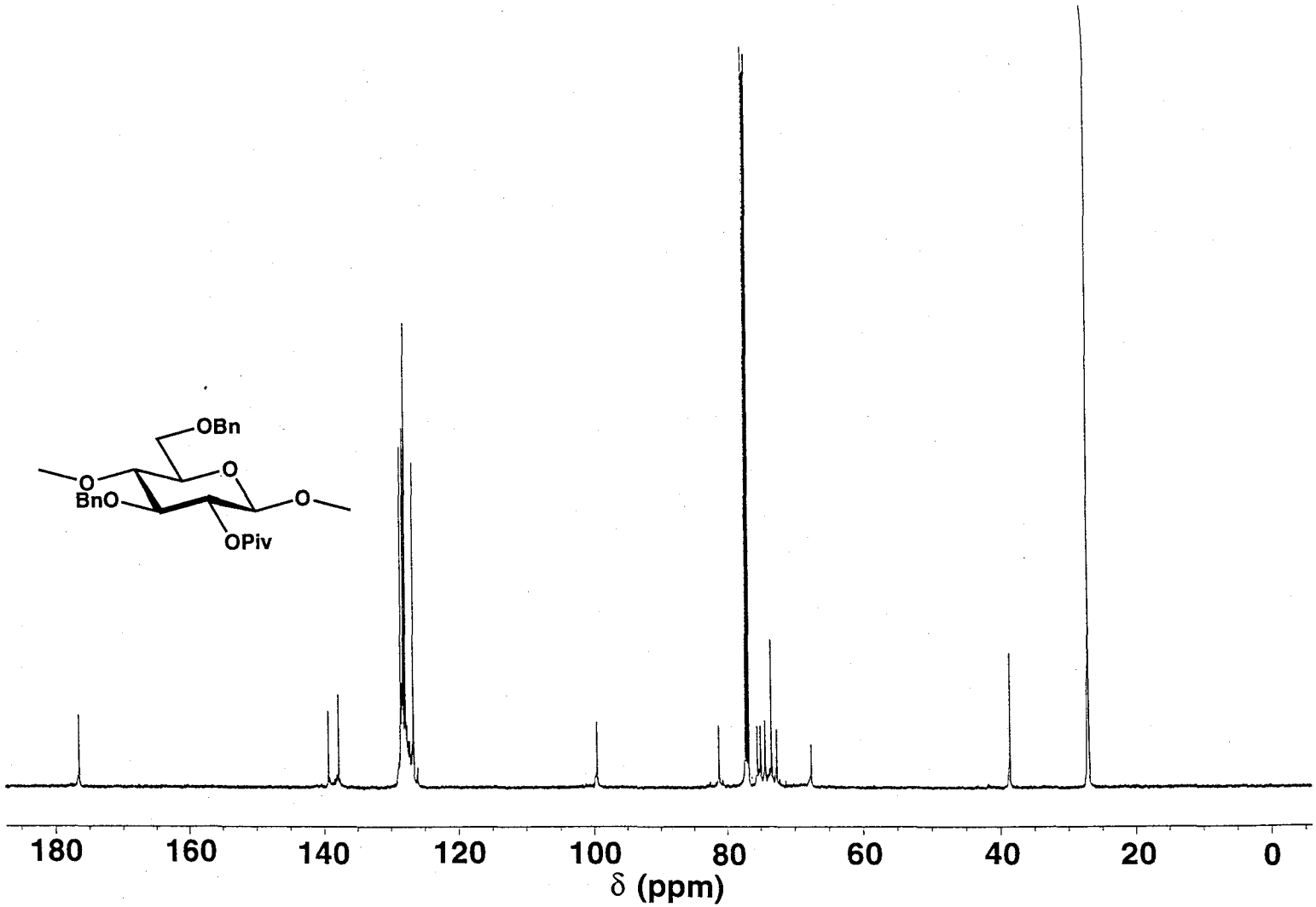


Figure 9. 125-MHz ^{13}C-NMR spectrum of 3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranan poly(**5**) ($CDCl_3$ as solvent).

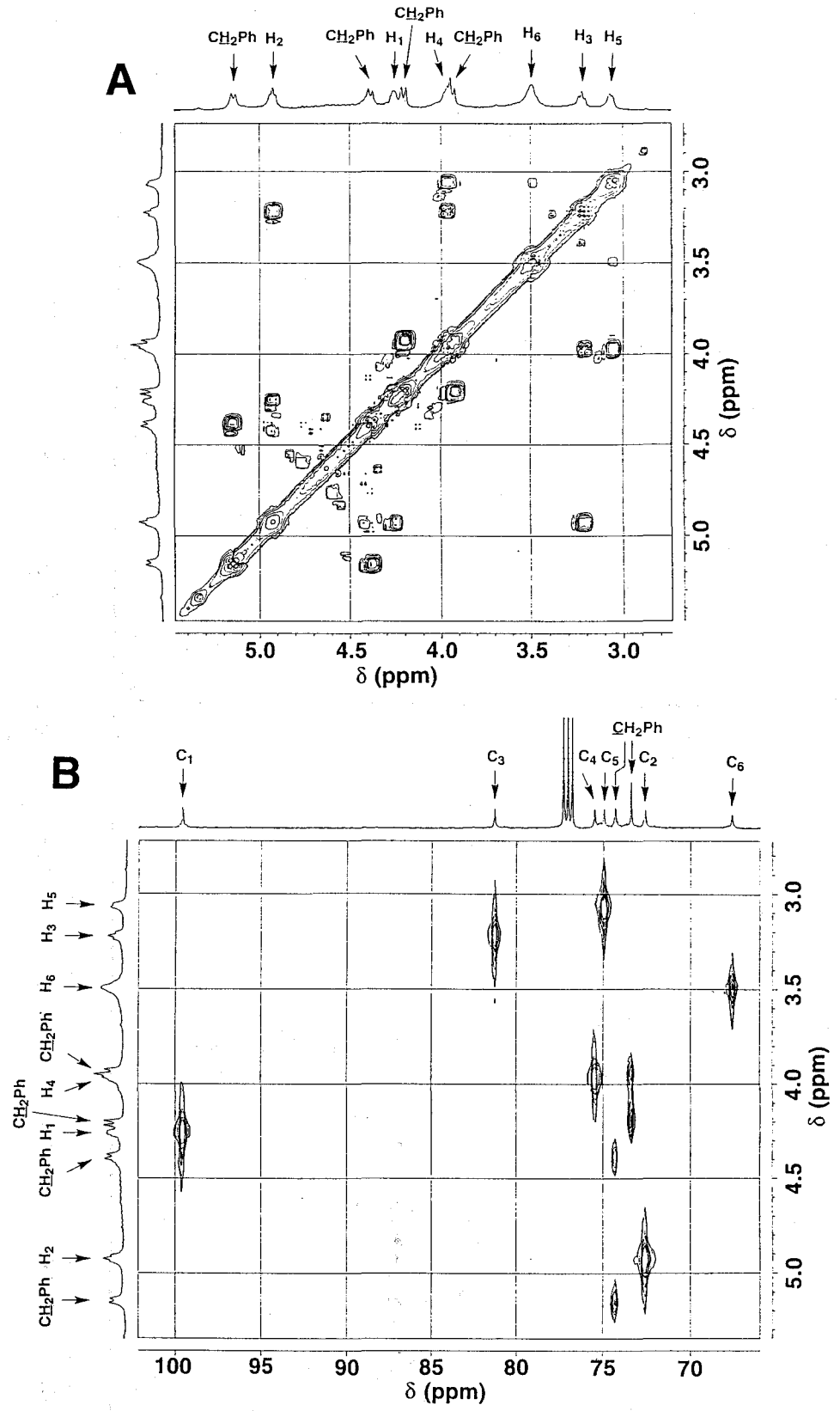


Figure 10. 2D-NMR spectra of 3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranan poly(**5**): (A) plot from H-H COSY experiment and (B) plot from C-H COSY experiment ($CDCl_3$ as solvent).

Table 9. Chemical Shift of 3,6-Di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranan (**6**)

carbon no.	1	2	3	4	5	6	3-*O*-benzyl	6-*O*-benzyl
H	4.26	4.92	3.22	3.96	3.06	3.49	4.41 5.15	3.93 4.20
C	99.60	72.61	81.30	75.50	75.00	67.59	74.33	73.41

The value of the coupling constant of C_1-H appearing at δ 4.23 is 8.7 Hz calculated from the $J_{1,2}$-value of C_2-H. This indicates β-glucosidic linkages between the repeating units in poly(**5**)s; the value would be about 3.0 Hz in the case of α-glucosidic linkages. [44] The β-glucosidic linkage is also supported by a sharp peak assigned to the C_1-carbon appearing at 99.60 ppm in ^{13}C-NMR. The chemical shift is very close to that (C_1' δ 99,50 ppm) of the cellobiose derivative, allyl 3,6,3',6'-tetra-*O*-benzyl-2,2'-di-*O*-pivaloyl-β-D-cellobioside, obtained in our previous study. [18a] Furthermore, the high negative specific rotation of poly(**5**)s also supports β-glucosidic linkages in the polymer. Thus, all above results strongly indicate that the poly(**5**)s is a (1→4)-β-D-glucopyranan derivative.

4.1.2 Determination of structures of poly(6)s, poly(7)s, and poly(8)s synthesized from 6, 7, and 8, respectively

There are four possible structural units in the poly(D-glucose) prepared by ring-opening polymerization of α-D-glucopyranose 1,2,4-orthoester derivatives, namely, the (1→4)-β- ((1→4)-β-P) and (1→4)-α-D-glucopyranosidic ((1→4)-α-P) units and the (1→2)-β- ((1→2)-β-P) and (1→2)-α-D-glucopyranosidic ((1→2)-α-P) units.

^{13}C-NMR spectrum (Figure 11A) of poly(**6**) having $[\alpha]_D$ -3.7° (Table 10, experiment no. 5) shows a single anomeric peak at 100.1 ppm, indicating a stereoregular poly(**6**). In a similar manner, the C-1 peak of the celloeicosaose derivative with the same protective group system (benzyl group at the 3-*O* position, and pivaloyl groups at the 2-*O* and 6-*O* positions) appears at 100.1 ppm. [19c] In addition, other carbon resonances of the stereoregular poly(**6**) are completely agreed with those of the celloeicosaose derivative. Thus, it is concluded that the stereoregular poly(**6**) is a (1→4)-β-D-glucopyranan derivative, *i.e.*, cellulose derivative.

^{13}C-NMR spectrum (Figure 11B) of poly(**7**) having $[\alpha]_D$ -12.6° (Table 10, experiment no. 8) shows triple anomeric peaks at 98.6 ppm (major), 98.3, and 98.9 ppm (minor; their height is almost same with each other.) indicating a non-stereoregular poly(**7**). The poly(**7**) was converted to an acetyl derivative in order to

Table 10. Polymerization of α-D-Glucopyranose 1,2,4-Orthopivalate Derivatives[a]

exp. no.	monomer	initiator	temp, °C	time h	yield, %	$[\alpha]_D$, deg	10^{-3} M_{GPC}	$\overline{DP_n}$
1	**5**	Ph_3CBF_4	-30	16	50	-20.1	2.9	6.9
2	**5**	Ph_3CBF_4	0	18	96	-32.9	3.8	8.9
3	**5**	Ph_3CBF_4	20	14	93	-35.2	4.5	10.5
4	**6**	Ph_3CBF_4	-30	96	21	-1.4	4.1	9.7
5	**6**	Ph_3CBF_4	0	22	51	-3.7	4.9	11.6
6	**6**	Ph_3CBF_4	20	2	60	+1.9	3.2	7.5
7	**7**	Ph_3CBF_4	-30	96	33	-26.8	2.9	6.9
8	**7**	Ph_3CBF_4	0	49	47	-12.6	3.7	8.8
9	**7**	Ph_3CBF_4	20	15	58	-18.8	3.0	7.1
10[b]	**8**	Ph_3CBF_4	-30	97	trace			
11[b]	**8**	Ph_3CBF_4	0	96	trace			
12[b]	**8**	Ph_3CBF_4	20	17	17	-24.8	1.4	3.5

a) Initiator concentration: 5 mol %; soluvent: CH_2Cl_2; monomer / solv. 50 g / 100 mL.

b) monomer / solv. 25 g / 100 mL.

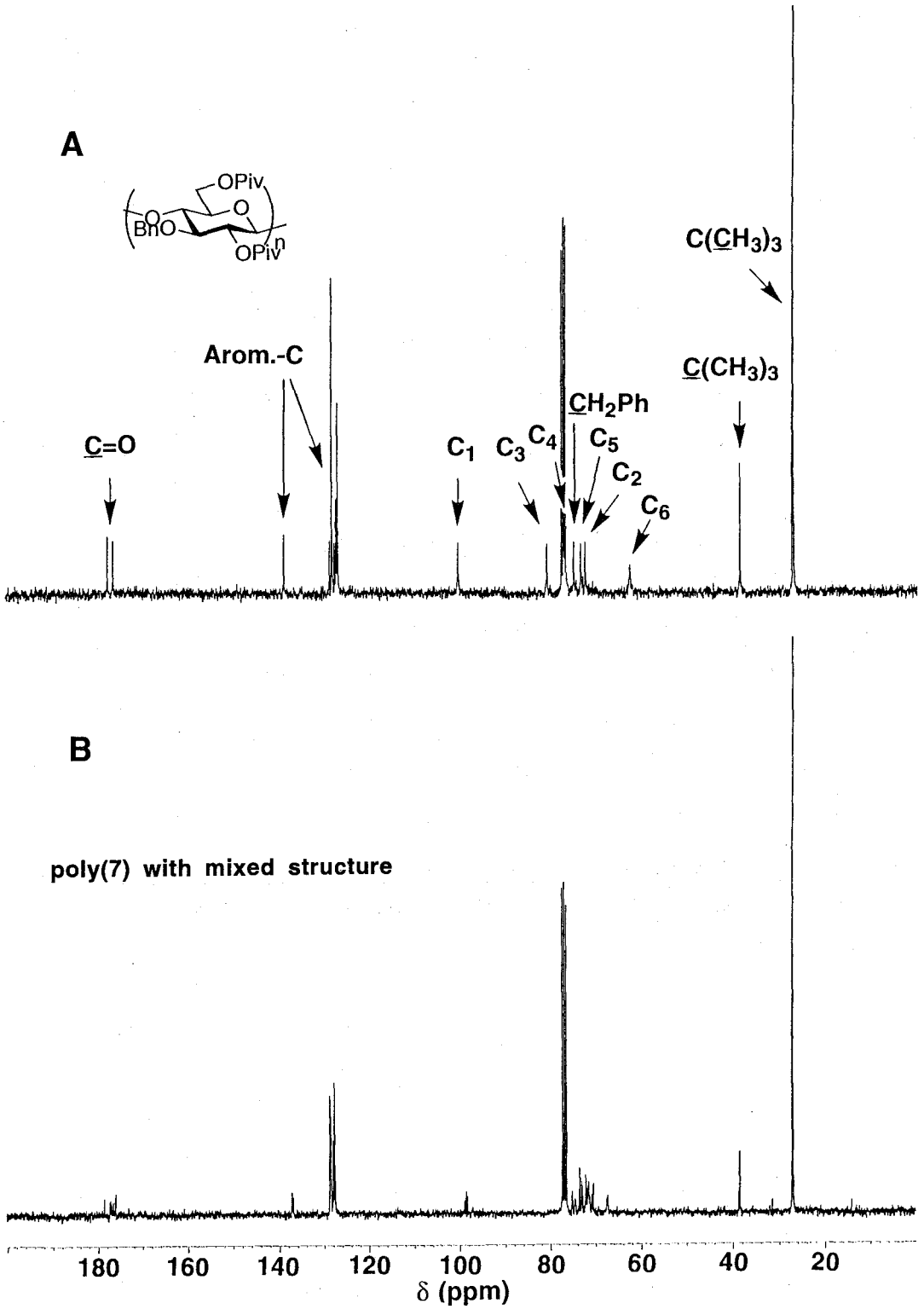


Figure 11. 75-MHz ^{13}C-NMR spectra of (A) poly(**6**) polymerized at 0°C (Table 10, experiment no. 5), and (B) poly(**7**) polymerized at -30°C (Table 10, experiment no. 7) ($CDCl_3$ as solvent).

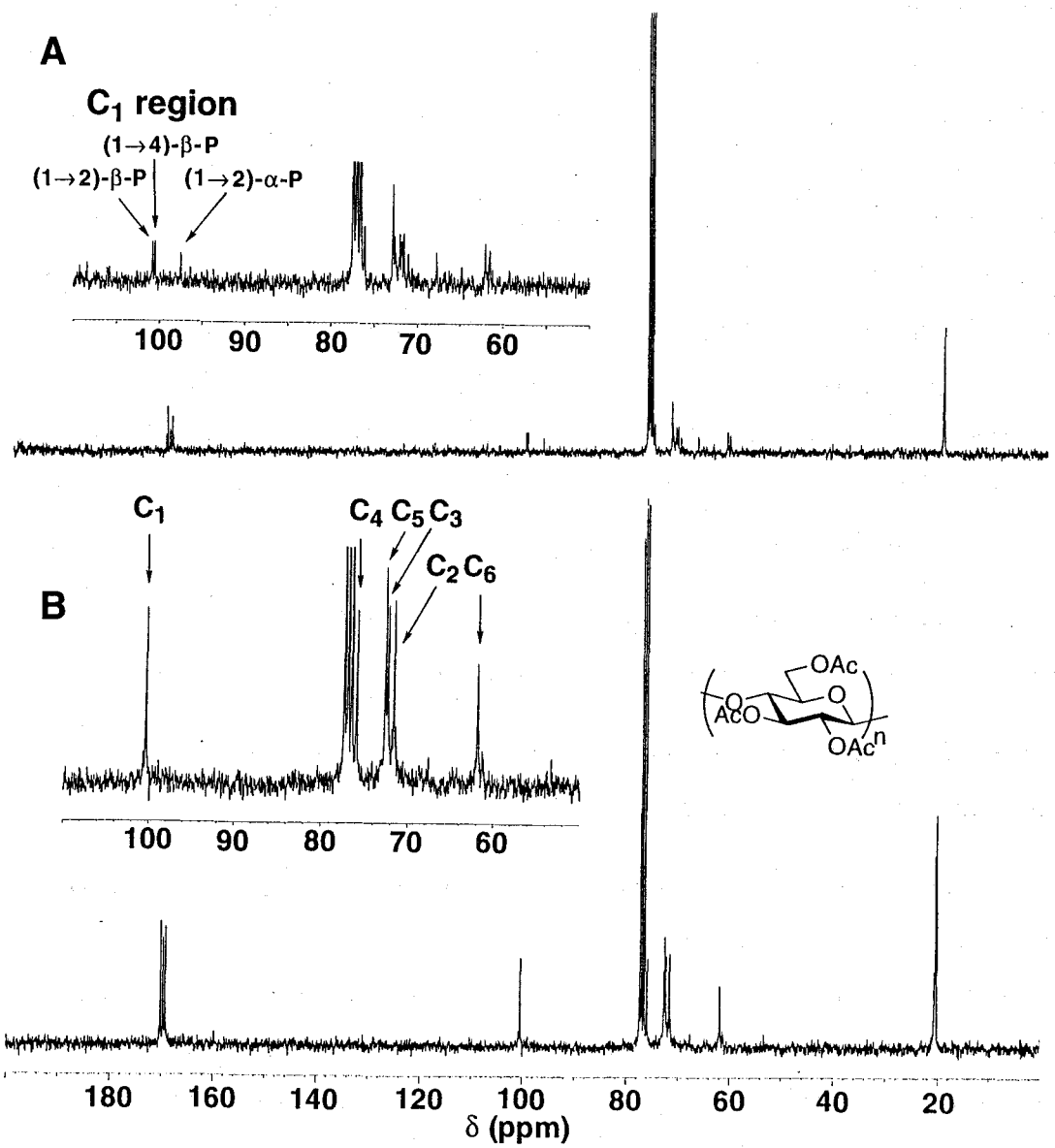


Figure 12. 75-MHz ^{13}C-NMR spectra of (A) acetylated poly(**7**) polymerized at -30°C (Table 10, experiment no. 7), and (B) cellulose triacetate synthesized from poly(**5**) polymerized at 20°C ($CDCl_3$ as solvent).

determine its structure. The anomeric peaks of the acetylated poly(**7**) appeared at 97.6, 100.5, and 100.8 ppm, as shown in Figure 12A. On the other hand, the anomeric peaks of an amylose acetate ((1→4)-α-P) and a cellulose acetate ((1→4)-β-P) appear at 95.7 and 100.5 ppm, respectively. In addition, an anomeric peak of methyl 3,4,6-tri-*O*-acetyl-2-*O*-methyl-α-D-glucopyranose, which is a model compound of a (1→2)-α-P unit, appears at 97.7 ppm [45], and an anomeric peak of non-reducing end group of β-sophorose octaacetate (1,3,4,6-tetra-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranose), which is a model compound of a (1→2)-β-P unit, appears at 100.8 ppm [46]. Therefore, the anomeric peaks of acetylated poly(**7**) at 97.6, and 100.5 ppm were assigned to (1→2)-α-P, and (1→4)-β-P units, respectively. The anomeric peak at 100.8 ppm of acetylated poly(**7**), compared with cellulose triacetate, was assigned to (1→2)-β-P units as shown in Figure 12. Polymerization of **7** produced no (1→4)-β-P unit. A structure of poly(**8**) was, however, unidentified because polymerization of **8** did only afford a polymer with a low molecular weight in a low yield.

4.2 Substituent effect on ring-opening polymerization of α-D-glucopyranose 1,2,4-orthopivalate derivatives

4.2.1 Ring-opening polymerization of 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (5)

Polymerization of the orthoester **5** was carried out under several reaction conditions: at different temperatures (-30 to 20 °C), in the presence of different catalysts (PF_5, BF_3-Et_2O, Ph_3CSbCl_6, Ph_3CBF_4) at 5 mol % concentration, at different monomer concentrations (25 - 100 g / 100 mL). Methylene chloride was the best solvent among those tried. A portion of the results is summarized in Table 8. The molecular weight of the polymer increases with an increase of monomer concentration. In the polymerization catalyzed by Ph_3CBF_4, increasing temperature tends to increase the molecular weight of the polymer, but the opposite tendency was obtained in the case of Lewis acids other than Ph_3CBF_4. The best result was obtained using Ph_3CBF_4 catalyst, that is, the highest $\overline{DP_n}$ was approximately 20 (Table 8, experiment no. 9). All polymers obtained are levorotatory and the absolute value

gradually increases with increase of molecular weight, but tends to converge to approximately -40°. These large negative specific rotations clearly indicate that these polymers have β-configuration. In fact, all these polymers were proved to be stereoregular (1→4)-β-D-glucopyranan by ^{13}C-NMR analyses as described in a section (**4.1.1**).

4.2.2 Ring-opening polymerization of 3-*O*-benzyl-6-*O*-pivaloyl- (6), 6-*O*-benzyl-3-*O*-pivaloyl- (7), and 3,6-di-*O*-pivaloyl- (8) α-D-glucopyranose 1,2,4-orthopivalates

The results of polymerizations of α-D-glucopyranose 1,2,4-orthopivalate derivatives **6**, **7**, and **8** are summarized in Table 10, which contains the partial results from **5**. For comparing temperature-dependence among the four monomers, all polymerizations were carried out under Ph_3CBF_4 as an initiator, the same initiator concentration (5 mol %), and the same monomer concentration (50 g / 100 mL) except for those of monomer **8**. Monomer **8** is difficult to be dissolved in the same monomer concentration, because monomer **8** has low solubility and a relatively high melting point (*ca.* 128 °C): monomer **5**; *ca.* 59 °C, monomer **6**; *ca.* 73.5 °C, monomer **7**; *ca.* 86.5 °C. Thus, polymerization of monomer **8** carried out in low monomer concentration (25 g / 100 mL).

Polymerizations of **5**, **6**, and **7** gave polysaccharide with almost same degree of polymerization ($\overline{DP_n}$). Number-averaged molecular weights of Poly(**5**)s, Poly(**6**)s, and Poly(**7**)s, determined by gel permeation chromatography using polystyrene standards, ranged from 2.9×10^3 to 11.6×10^3. However, polymerizability of **8** was extremely low among four monomers. When compound **8** was polymerized at 20 °C, unreacted monomer (approximately over 70%) was remained in a reaction ampule; none of monomers **5**, **6**, and **7** was not remained under the same reaction conditions. Polymerization of **8** did only afford an oligo-saccharide in a low yield.

Poly(**6**)s have a stereoregular structure, as shown in Figure 11A. However, poly(**6**)s tend to have a specific rotation of almost around 0°. The rule that a polysaccharide having a large specific rotation is stereoregular does not fold for this

special case. This data agreed with those of cellooligosaccharides with the same protective group system (benzyl group at the 3-*O* position, and pivaloyl groups at the 2-*O* and 6-*O* positions) [18]. On the other hand, poly(**7**)s are levorotatory between *ca.* -12° and -27°. Although poly(**7**) has higher negative specific rotation than poly(**6**), the polymer has a non-stereoregular structure, as shown in Figures 11 and 12.

4.2.3 Substituent effect on molecular weight of polysaccharides

Molecular weights of poly(**5**)s, poly(**6**)s, and poly(**7**)s are almost the same as each other, but those of poly(**8**)s were low under all reaction conditions tried. The polymerizability of four monomers is in the order of **5** ≅ **6** ≅ **7** >> **8**, as judged from the highest molecular weight and yield obtained from these monomers (Table 10, experiment nos. 3, 5, 8, and 10). It can be said that polymerizability of **8** could not be compared exactly with those of **5**, **6**, and **7** because polymerization of **8** was conducted in the different concentration with those of **5**, **6**, and **7**, but the above mentioned trend must be true and substantial.

In cases of ring-opening polymerizations of 1,4-anhydro-α-D-glucopyranose derivatives, the benzyl group at the 3-*O* position is indispensable for yielding glucan with high molecular weight. However, in the present cases of those of α-D-glucopyranose 1,2,4-orthopivalate derivatives, the benzyl group at the 3-*O* position is indispensable for realizing the stereoregularity, but is *dispensable* for yielding glucan with high molecular weight: that is, monomer **7** having pivaloyl group at 3-*O* position polymerized well but without yielding stereoregularity. The reason why 3-*O*-benzyl group is *dispensable* in this case could be ascribed to the fact that the complexation of catalyst with a C_3-oxygen would not tend to take place because a C_3-substituent group of α-D-glucopyranose 1,2,4-orthopivalate derivative is axially attached on $^3S_1$-conformation and is far from a C_4-oxygen or a C_2-oxygen with which catalyst would coordinate.

Monomers having one benzyl group and two pivaloyl groups (including a orthopivaloyl group), that is, monomers **6** and **7** had same polymerizability as monomer **5** having two benzyl group and one pivaloyl group. Monomer **8**, however, had

remarkably low polymerizability among four monomers. Consequently, the fact that monomer has one benzyl group is indispensable for yielding a polymer with high molecular weight.

4.2.4 Substituent effect on stereoregularity of polysaccharides

Polymerizations of **5** and **6** having 3-*O*-benzyl group gave stereoregular (1→4)-β-D-glucopyranan derivatives (Table 10, experiment nos. 1-6). However, polymerizations of **7** did afford a stereo-irregular polysaccharide consisting of (1→2)-α-P, (1→4)-β-P, and (1→2)-β-P units. A (1→2)-bond formation increased with an decrease in temperature. That is, while probability of coordination of Ph_3CBF_4 with a C_2-oxygen was equal to that with a C_4-oxygen at 20 °C and 0 °C, the coordination with the C_2-oxygen took place in preference to that with the C_4-oxygen at -30 °C: (1→2)-α-P / (1→4)-β-P / (1→2)-β-P = 1 : 2 : 1 (Table 10, experiment nos. 8 (20 °C) and 9 (0 °C)); (1→2)-α-P / (1→4)-β-P / (1→2)-β-P = 3 : 4 : 3 (Table 10, experiment no. 7 (-30 °C)). This fact also indicates that in case of coordination of a catalyst with the C_2-oxygen, probability of an α-side attack resulting in formation of (1→2)-α-P was equal to that of a β-side attack resulting in formation of (1→2)-β-P.

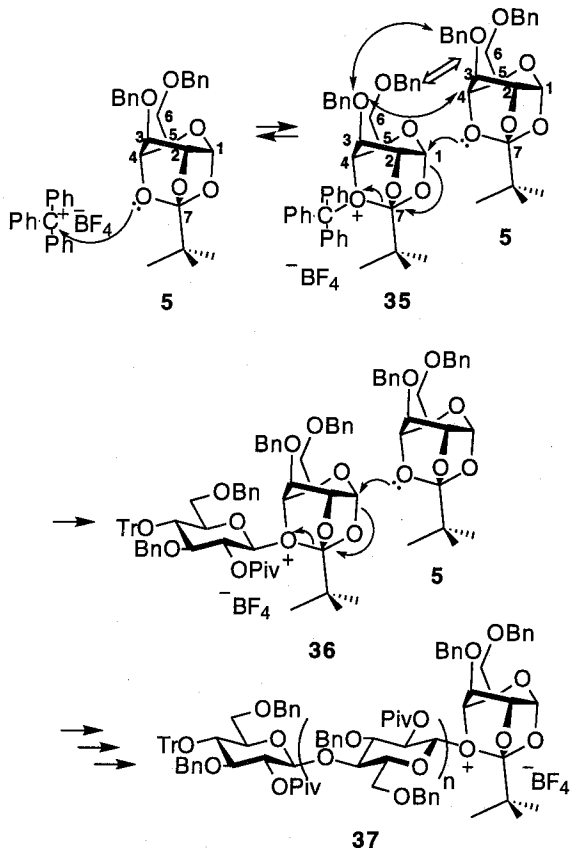
After all, the benzyl group at the 3-*O* position is indispensable for yielding a stereoregular cellulose derivative, *i.e.*, a (1→4)-β-D-glucopyranan derivative synthesized from α-D-glucopyranose 1,2,4-orthopivalate derivatives. This fact agreed with the case for yielding a stereoregular (1→5)-β-D-glucofuranan derivatives synthesized from 1,4-anhydro-α-D-glucopyranose derivatives.

4.2.5 Mechanism of polymerization

The trialkyloxonium ion mechanism shown in Scheme 10 has been proposed for the stereoregular ring-opening polymerization of 1,4- and 1,6-anhydro sugars. [10b, 10c, 14, 15] First of all, in the initiation step of this mechanism, an oxonium ion intermediate (**35**) is formed by the complexation of a triphenylcarbenium ion with oxygen at the C_4-position (C_4-O). Then, the β-side attack of the next monomer **5** with Walden inversion at the C_1-position of the oxonium ion intermediate (**35**) accompanied by the scissions

of the C_4-O-C_7 and C_1-O-C_7 bonds, results in the formation of a dimeric trialkyloxonium ion **36**. Subsequently, in the propagation step, the continuous attacks of the monomer **5** on the trialkyloxonium ion afford a polymeric trialkyloxonium ion **37** consisting of a (1→4)-β-D-glucopyranan chain.

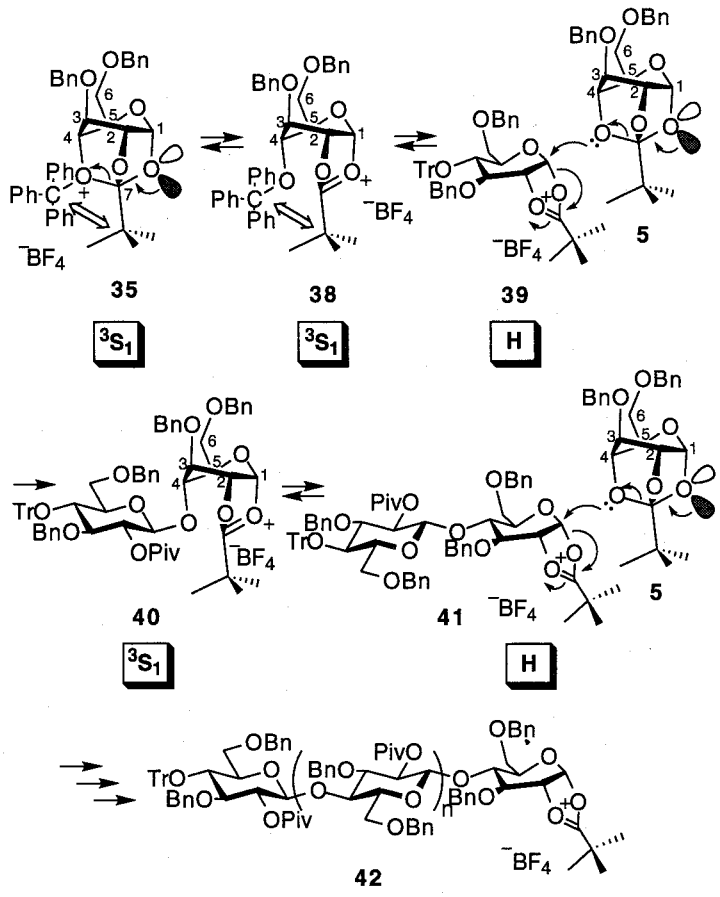
However, the β-side attack of the next monomer **5** on the oxonium ion **35** may be difficult because of the steric hindrance of the axial 3-*O*-benzyl group in the oxonium ion **35** having a $^3S_1$-conformation; the situation is also the same at the propagation step. Consequently, the present ring-opening polymerization may be explained by the dioxalenium ion mechanism (Scheme 11) [10] rather than the trialkyloxonium ion mechanism.



Scheme 10. Trialkyloxonium ion mechanism

The oxonium ion intermediate **35** formed at the initiation step is thought to be immediately converted to a dioxalenium ion **38** by the intramolecular back-side attack

of a lone pair orbital on the C_1- or C_2-oxygens oriented antiperiplanar to the C_4O-C_7 bond in preference to the attack of monomer **5** because of instability caused by the large steric repulsion between the C_4O-trityl and the C_7-*t*-butyl groups. The metastable ion **38** with $^3S_1$-conformation seems to stabilize to another dioxalenium ion **39** with a half-chair (H) conformation, where both the 3-*O*- and C_6-*O*-benzyl groups have the more stable equatorial orientation. The intermediate **39** can then undergo an intermolecular reaction with next monomer **5** without any hindrance from the axial 3-*O*-benzyl group like that in Scheme 10, resulting first in a dimeric dioxalenium ion **40** with $^3S_1$, which then stabilizes to **41** in the H-form.



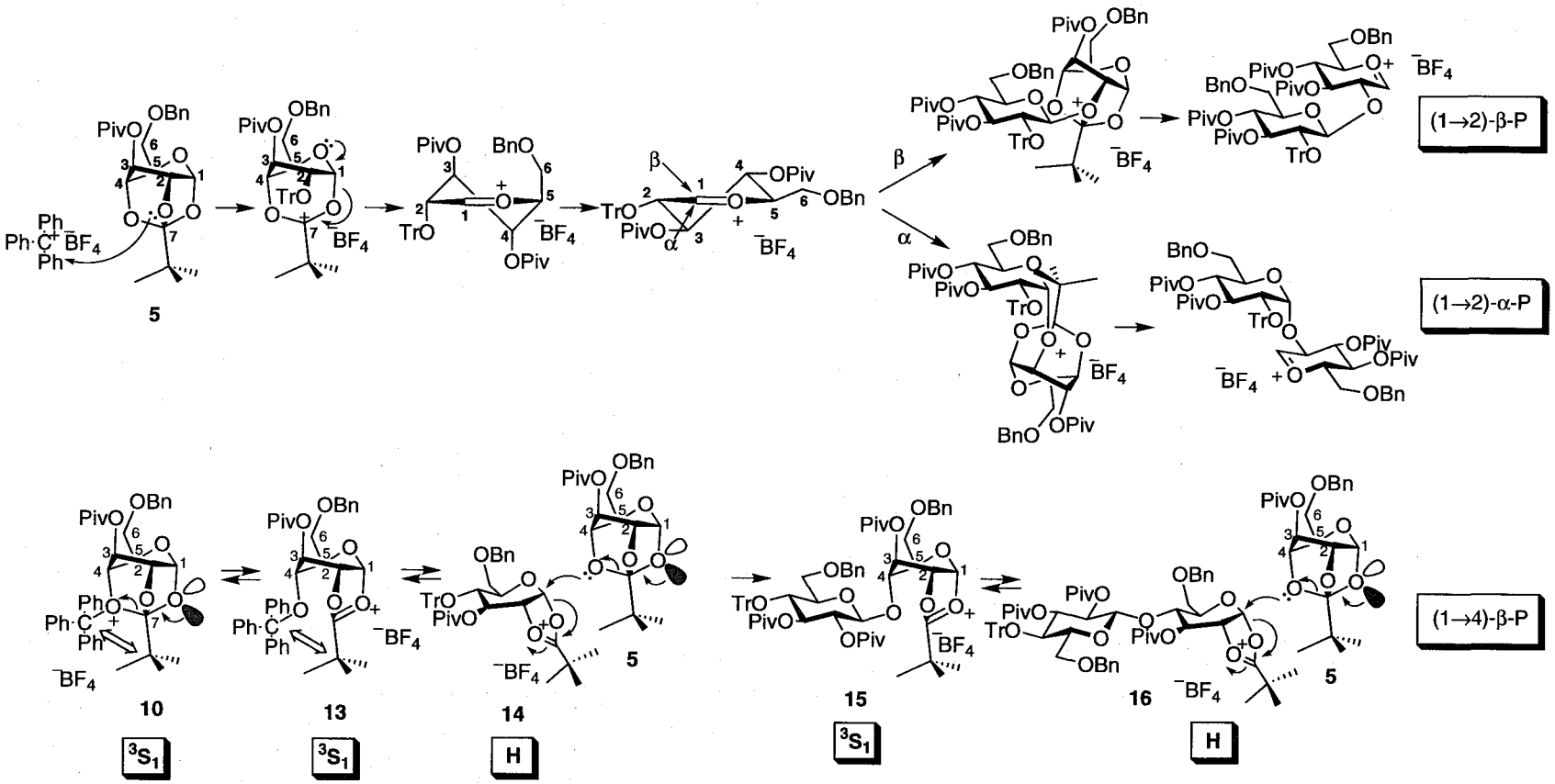
Scheme 11. Dioxalenium ion mechanism

In the propagation step, the β-side attack of next monomer **5** on the reducing end of the elongating chain and conformational transformation of $^3S_1$ into H-conformation are alternatively repeated stepwise to afford a polymeric dioxalenium ion **42**. Finally,

one mole of water is introduced into the **42** at the work-up step to give a completely stereoregular (1→4)-β-D-glucopyranan derivative. The mechanism in Scheme 11 is quite similar to that of the exclusive formation of low molecular weight 1,2-trans glycoside using the neighboring participation of a 2-*O*-acyl group. [10a, 47] The trityl group of the non-reducing end may be removed by hydrolysis with strong acid formed during work-up.

Generally, there are two possible ring-opening modes, 1,2 and 1,4 scissions, in the cationic ring-opening polymerization of tricyclic 1,2,4-orthoester. Quantum chemical calculations showed that electrophilic attacks at these two centers, the C_2-*O*- and C_4-*O*-positions, giving (1→2)- and (1→4)-glucans, respectively, are expected to be of nearly equal probability. [48] In fact, Bochkov *et al.* prepared xylan from 3-*O*-acetyl-α-D-xylopyranose 1,2,4-orthoacetate under optimum conditions containing an approximately equal number of (1→2)-α- and (1→4)-β-glycosidic linkages. [10a, 49] Furthermore, the production of a 1,4-anhydro sugar and its polymerization also have been reported as side reactions in the ring-opening polymerization of a 1,2,4-orthoester. [50] However, none of these side reactions occurred in the present polymerization of monomer **5**. If the conversion of monomer **5** into anhydro sugar **2** occurred, the product should be a stereoregular (1→5)-β-D-glucofuranan poly(**2**)', but such possibility was refuted by the analyses of the ^{1}H- and ^{13}C-NMR spectra of the product.

Comparing the present results with those of 3-*O*-acetyl-α-D-xylopyranose 1,2,4-orthoacetate, the 3-*O*-benzyl group of monomer **5** is found to play an extremely important role in yielding a completely stereoregular (1→4)-β-D-glucopyranan. It is reasonably explained that the electron-donating effect of the 3-*O*-benzyl group affects an increase of the electron-density of the oxygen at the C_4-position, whereupon a triphenylmethylcarbenium ion preferentially complexes with the C_4-oxygen, not the C_2-oxygen, resulting in the formation of a stereoregular (1→4)-β-D-glucopyranan *via* the oxonium ion intermediate **35**.

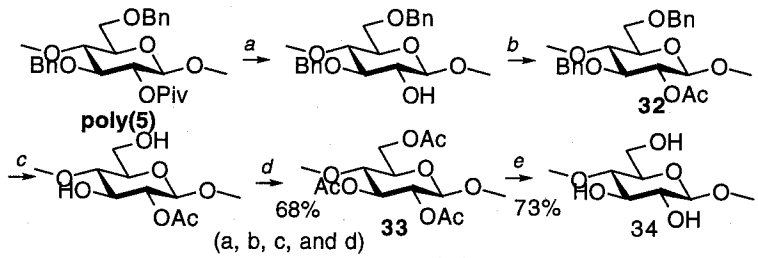


Scheme 12

In addition, Scheme 12 illustrates the proposed mechanism of polymerization of **7** resulting in poly(**7**)s with mixed structures. In the case of (1→2)-bond formation, the coordination of the catalyst with the C_2-oxygen affords a seven-membered ring carbonium-ion intermediate, which is unstable so that C_1-O_7 bond breaking must precede an attack of next monomer to afford a subsequent planar carboxonium-ion intermediate, in which consequently the next monomer attacks C_1 carbon from both sides of the planar intermediate with equal probability because there is no neighboring participations caused by both C_3- and C_4-pivaloyl groups. Thus, the above mentioned mechanism makes production of almost the same amount of (1→2)-α- and (1→2)-β-P units.

Decrease of electron density of a C_4-oxygen by a pivaloyl group at a 3-*O* position is supported by ^{1}H-NMR data of orthoester derivatives (Table 7): C_4-protons of monomers **7** and **8** are unexpectedly deshielded to appear at 5.08 and 5.12 ppm. Highly regioselective coordination of the catalyst with the C_4-oxygen yields stereoregular polysaccharide.

4.3 Conversion of the poly(5)s into cellulose (34) *via* cellulose triacetate (CTA) (33)



[a] $NaOCH_3$ / THF:MeOH (10:1) / reflux / over night, [b, d] $(CH_3CO)_2O$ / pyridine / r.t. / over night,

[c] H_2 / $Pd(OH)_2$ on carbon / THF:AcOH (1:1) / 4.5kgf/cm^2 / r.t. / 3h, [e] $NaOCH_3$ / THF:MeOH (10:1)/r.t./48h

Scheme 13. Conversin of the poly(**5**)s into cellulose (**34**) *via* cellulose triacetate (CTA) (**33**).

Stereoregular Poly(**5**)s was converted to a cellulose (**34**) as shown in Scheme 13. First, poly(**5**)s was converted into its 2-*O*-acetyl derivative (**32**) by treating with $NaOCH_3$ in THF / methanol (10 / 1, v / v) at reflux, and then with acetic anhydride and pyridine. The ^{1}H-NMR spectra of poly(**5**)s and **32** were completely identical except for the peaks from pivaloyl and acetyl groups. Polymer **32** was then transformed into

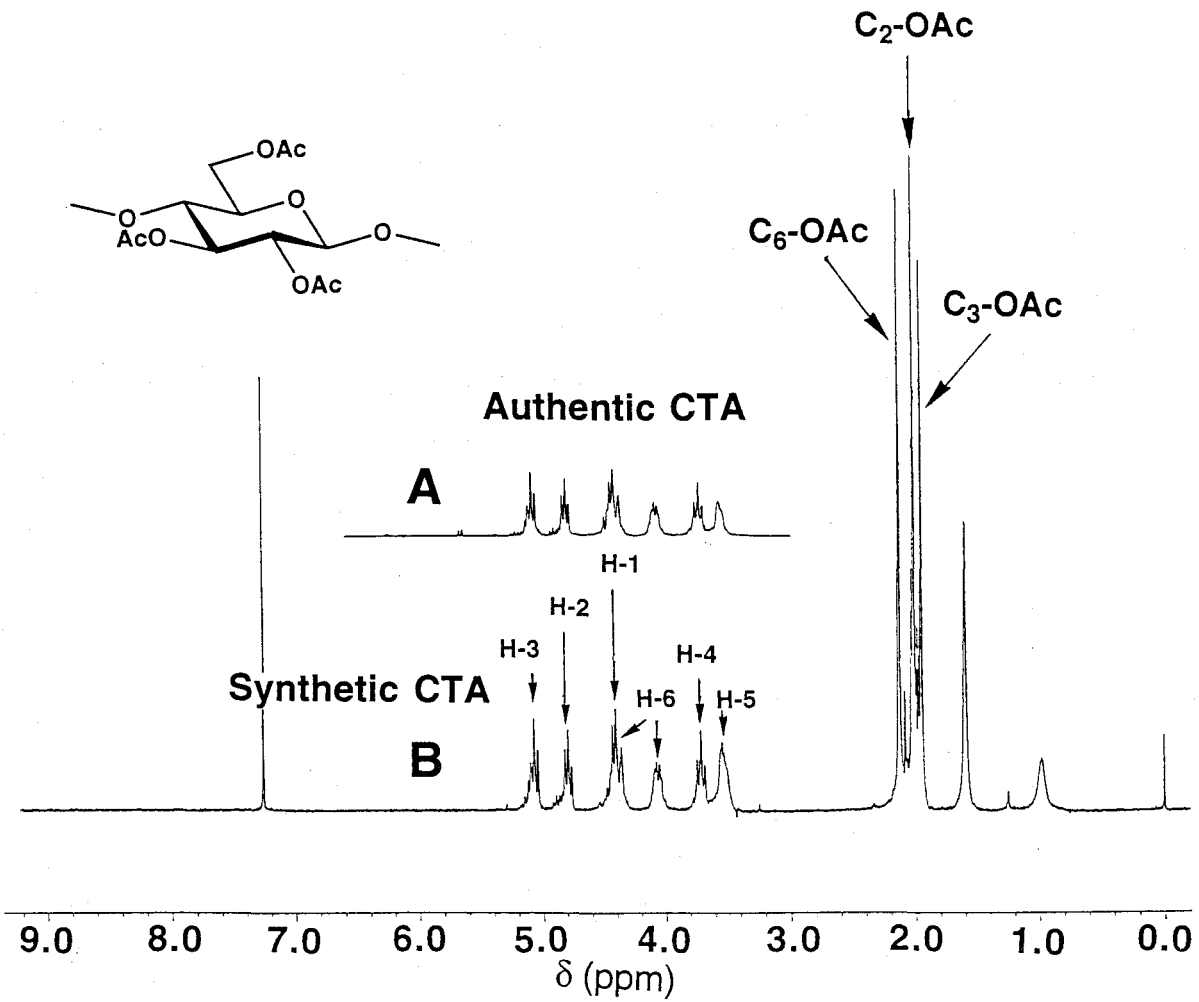


Figure 13. 300-MHz ^{1}H-NMR spectra of (A) authentic cellulose triacetate and (B) synthetic cellulose triacetate (**33**) ($CDCl_3$ as solvent).

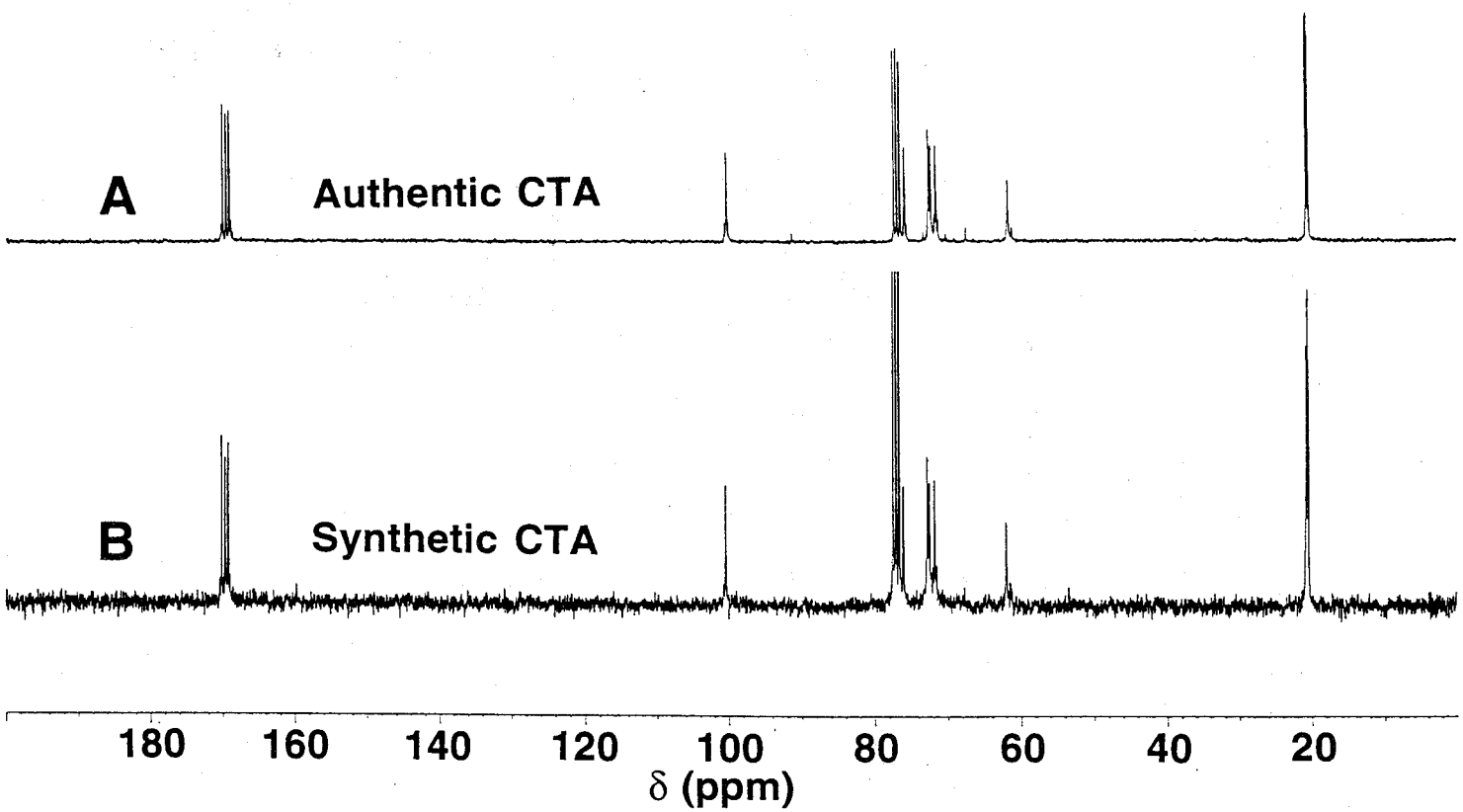


Figure 14. 75-MHz ^{13}C-NMR spectrum of (A) authentic cellulose triacetate and (B) synthetic cellulose triacetate (**33**) ($CDCl_3$ as solvent).

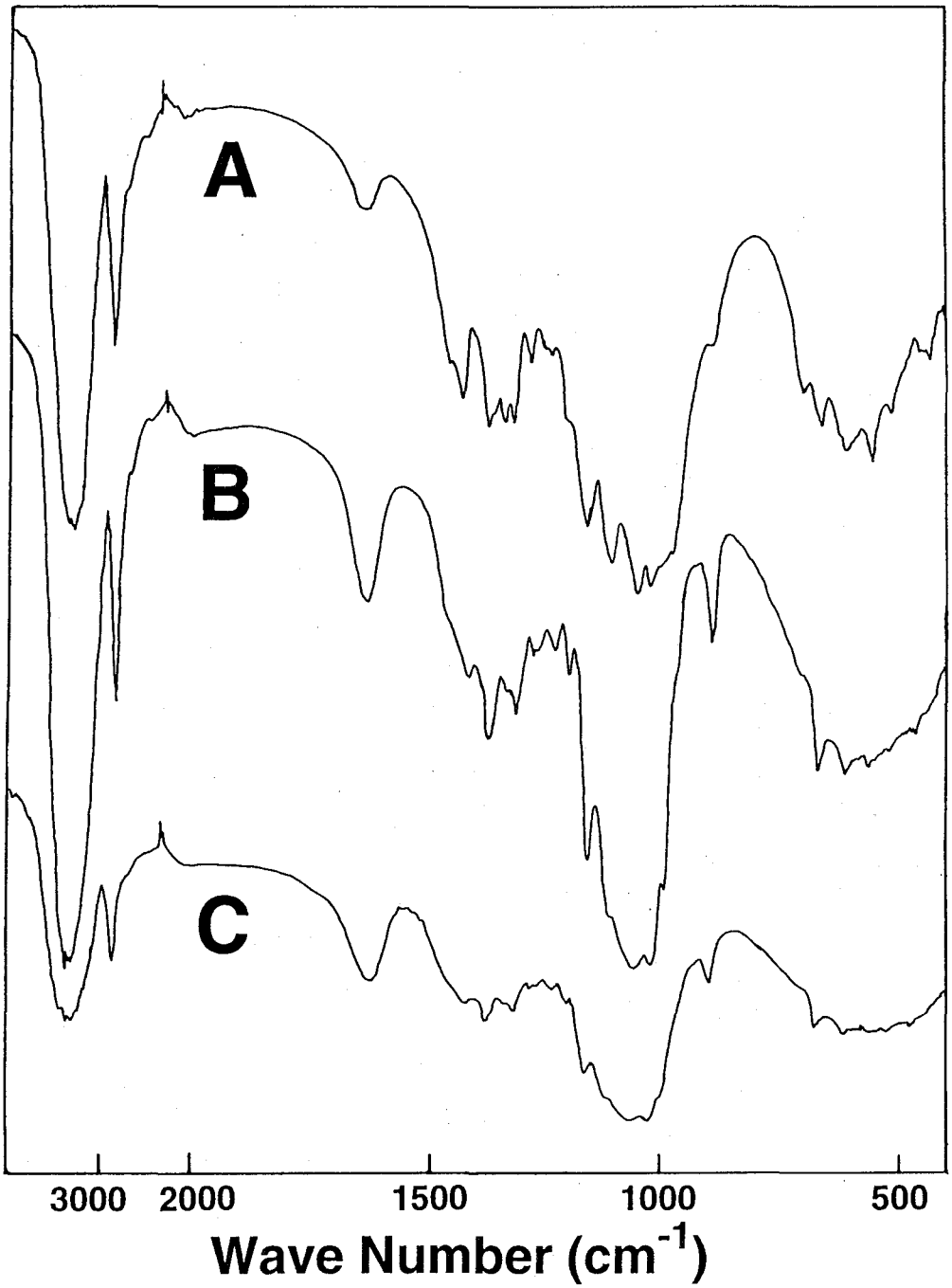


Figure 15. IR spectra of (A) Whatman® cellulose CF11 (cellulose-I), (B) regenerated cellulose (cellulose-II), and (C) synthetic cellulose (cellulose-II).

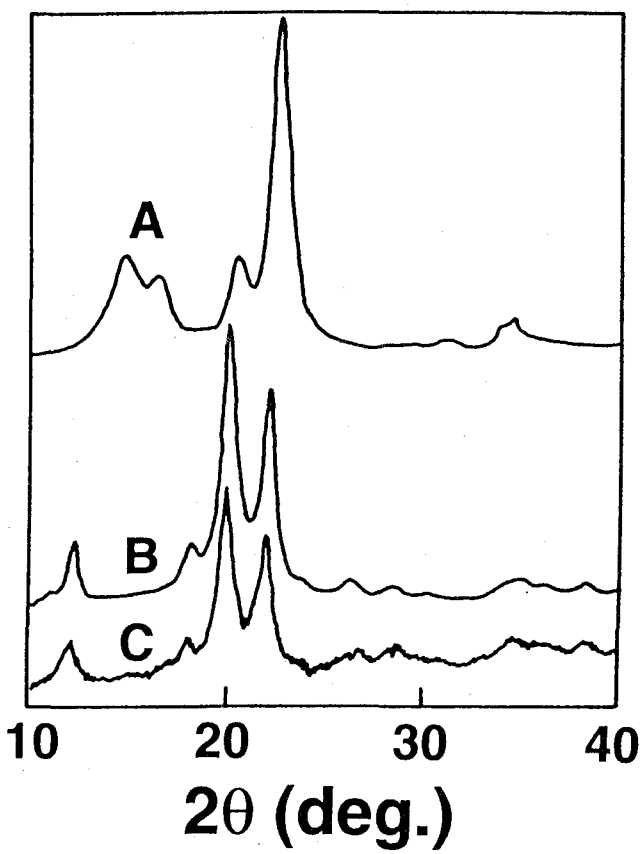


Figure 16. X-ray diffractograms of (A) Whatman® cellulose CF11, (B) regenerated cellulose, and (C) synthetic cellulose.

CTA (**33**) by debenzylation with H_2 in the presence of palladium hydroxide on carbon under 4.5 kg / cm^2 pressure and then acetylation with acetic anhydride and pyridine. The degree of polymerization of the CTA (**33**) was almost in agreement with that of poly(**5**)s: depolymerization did not occur during the deprotection processes. The ^{1}H- and ^{13}C-NMR spectra of polymer **33** were completely identical with those of authentic CTA prepared from cellulose with low molecular weight (Figures 13 and 14, respectively) [51]; acetyl protons were completely identical with each other, but only ring protons are shown in Figure 13 for comparison.

Finally, the cellulose triacetate thus obtained was converted to cellulose by deacetylation with $NaOCH_3$ in THF / methanol (10 / 1, v / v). The IR spectrum and X-ray diagram of cellulose prepared in this way were completely identical with those of regenerated cellulose with the cellulose-II crystal structure [52] (Figures 15 and 16, respectively).

4.4 Summary

Selection of the best combination of protective groups for hydroxyl groups of sugars is very important for yielding highly selective glycosylation. Especially, the 3-*O*-benzyl group has been demonstrated to be indispensable to obtain (1→4)-β-glucosidic linkages with high stereoselectivity and in high yield from the stepwise synthesis of a series of cello-oligosaccharides. Furthermore, these substituent effects were also found in the synthesis of a stereoregular (1→5)-β-D-glucofuranan by ring-opening polymerization (Chapter 2). [28]

To investigate the substituent effects at the 3-*O*, and 6-*O* positions on ring-opening polymerization, 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**5**), 3-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**6**), 6-*O*-benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**7**), and 3,6-di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**8**) were selected as starting monomers and were polymerized under various reaction conditions. Substituted polymer was characterized by gel permeation chromatography, polarimetry, 2D-NMR spectroscopy, 1D ^{1}H- and ^{13}C-NMR spectroscopy. Polymerization of **5**, and **6** having

benzyl group at 3-*O* position afforded stereoregular (1→4)-β-D-glucopyranan derivatives, *i. e.*, cellulose derivatives. However, polymerization of **7** having pivaloyl group at 3-*O* position did not afford stereoregular polysaccharide.

Thus, it was concluded from results of monomers **5**, **6**, **7** and **8** in the author's present study that the benzyl group at the 3-*O* position is indispensable for yielding stereoregular (1→4)-β-D-glucopyranan derivatives, *i. e.*, cellulose derivatives. Mechanism of polymerization was discussed (Section **4.2.5**).

In addition, poly (**5**) was converted into cellulose *via* cellulose triacetate (Section **4.3**). Formation of cellulose was confirmed by ^{1}H- and ^{13}C-NMR spectroscopy, IR spectroscopy, and X-ray diffractometry. This is the first successful chemical entry into fully chemical synthetic cellulose.

After all, Taking into account such substituent effects, the author have now succeeded in the first syntheses of cellulose derivatives by cationic ring-opening polymerization, with conversion to cellulose by removal of the protective groups.

CONCLUSION

Cellulose is the most abundant natural organic polymer, existing as a main plant cell wall component, and is important as a biodegradable and renewable organic material. The synthesis of cellulose has been a very important, but extremely difficult, problem to be solved, since Schulbach first tried the synthesis.

On the other hand, there are many functional cellulose derivatives, which are industrially important materials. However, much remains unknown about the relationship between their structures and properties: which derivatives are more functional or active among those substituted at 2-*O*-, 3-*O*- or 6-*O*-positions. For these studies and for further molecular design of advanced materials from cellulose, it is imperative that the author develops methods that make it possible to prepare cellulose derivatives having functional groups at the desired positions among 2, 3, 6-hydroxyl groups in the repeating glucopyranose unit of cellulose.

The author has planned to synthesize a cellulose derivative by cationic ring-opening polymerization and has been able to get several successful results. Thus, the author's investigation would help to solve an above mentioned problem.

On the other hand, nobody has succeed in the synthesis of cellulose by ring-opening polymerization. However, there is a possibility of synthesizing the cellulose derivatives by ring-opening polymerization utilizing substituent effects. There is no report to investigate the influence of substituents for the acyl group and benzyl group in anhydro-sugar and sugar-orthoester skeletons except for the 2-*O* position. In this thesis, the author described substituent effects at the 2-*O*, 3-*O*, and 6-*O* positions on ring-opening polymerization for obtaining cellulose as a final goal by chemical synthesis.

In chapter 1 the author described synthetic routes for novel compounds 1,4-anhydro-2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose (**1**) 1,4-anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (**2**) [24], 1,4-anhydro-3-*O*-benzyl-2,6-di-*O*-

pivaloyl-α-D-glucopyranose (**3**), and 1,4-anhydro-6-*O*-benzyl-2,3-di-*O*-pivaloyl-α-D-glucopyranose (**4**) [25] having an acyl group (Figures 1, 2, 3, and 4, respectively). Compounds **1**, and **2** have one acyl group at C_6-, and C_2-position, respectively. On the other hand, compounds **3** and **4** have two acyl groups at C_2- plus C_6-positions, and C_2- plus C_3-positions, respectively. Compounds **1**, **2**, [24] **3**, and **4** [25] were given in a 57%, a 54%, a 46%, and a 63% yield, respectively. The author's method for obtaining 1,4-anhydro-α-D-glucopyranose derivatives was a large dilution one under mild acidic conditions, which cause intramolecular bond formation. The assignments of proton peaks were summarized in Table 1. A resonance of proton attached to a carbon, to which pivaloyl group is introduced, was shifted to a lower magnetic field.

In chapter 2, to investigate the substituent effects at the 2-*O*, 3-*O*, and 6-*O* positions on ring-opening polymerization, compounds **1**, **2** [24], **3**, and **4** [25] selected as starting monomers were polymerized under various reaction conditions: initiator-, solvent-, monomer concentration- and temperature-dependence.

Polymerization of **1** gave non-stereoregular polymers consisting of mainly (1→5)-α-D-glucofuranosidic units with $[\alpha]_D$ value of *ca.* +84° (Table 2). Polymerization of **2** with phosphorus pentafluoride catalyst produced new stereoregular polysaccharide derivatives, 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→5)-β-D-glucofuranans ($\overline{DP_n}$ = 42.6) with $[\alpha]_D$ value of *ca.* -66° (Table 3). Polymerization of **3** also produced (1→5)-β-D-glucofuranan derivative. Polymerization of **4**, however, gave non-stereoregular polysaccharides consisting mainly of (1→5)-β-D-glucofuranosidic units (Table 6). Substituted polymers were characterized by ^{1}H- and ^{13}C-NMR spectroscopy, polarimetry, and gel permeation chromatography.

Finally, it was concluded that both the pivaloyl group at the 2-*O* position and the benzyl group at the 3-*O* position were indispensable for yielding stereoregular (1→5)-β-D-glucofuranan derivatives with high molecular weight, and that a substituent group at the 6-*O* position hardly affects stereoregularity or polymerizability (Section **2.2.4**). The 1,4-anhydro-α-D-glucopyranose skeleton was not suitable for yielding a (1→4)-β-

D-glucopyranan, *i.e.*, cellulose. The mechanism of the ring-opening polymerization was discussed (Section **2.2.5**).

Furthermore, debenzylation and depivaloylation of the substituted polymers afforded unsubstituted (1→5)-β-D-glucofuranan (Section **2.3**). After all, the author has for the first time prepared the (1→5)-β-D-glucofuranan with $[\alpha]_D$ value of *ca.* -204°.

In chapter 3, synthetic methods of four new α-D-glucopyranose 1,2,4-orthopivalate derivatives were described. Novel four monomers 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (**5**), 3-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**6**), 6-*O*-benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**7**), and 3,6-di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (**8**) were synthesized from D-glucose in 8, 9, 5, and 6 reaction steps, respectively (Scheme 9).

Characteristics of the present new method exists in a final step. That is, substituent group at C_3- and C_6-position has already been introduced before a final step. Orthoesterification using *N,N'*-carbonyldiimidazole at the final step was carried out under a mild condition so that all protective groups were stable at that step. In addition, the new procedure could be widely applicable in the synthesis of a series of orthoester derivatives.

In the case of a previous method of Bochkov *et al.* [35] the rest free hydroxy groups would be substituted at a final step. However, the method was not applied to the syntheses of **6** and **7** because of a difficult distinction between C_3- and C_6- positions.

Taking into account total advantage, the present new method was more valuable than the previous method.

In chapter 4, to investigate the substituent effects at the 3-*O*, and 6-*O* positions on ring-opening polymerization, **5**, **6**, **7**, and **8** were polymerized under various reaction conditions (Tables 9 and 10). Substituted polymer was characterized by gel permeation chromatography, polarimetry, 2D-NMR spectroscopy, 1D ^1H- and ^{13}C-

NMR spectroscopy. Polymerizations of **5**, and **6** having the benzyl group at the 3-*O* position afforded stereoregular (1→4)-β-D-glucopyranan derivatives, *i.e.*, cellulose derivatives. However, polymerization of **7** having the pivaloyl group at the 3-*O* position did not give stereoregular polysaccharide.

Thus, it was concluded from results of monomers **5**, **6**, **7** and **8** that the benzyl group at the 3-*O* position is indispensable for yielding stereoregular (1→4)-β-D-glucopyranan derivatives, *i.e.*, cellulose derivatives. The reason for the indispensability and the mechanism of polymerization were discussed (Section **4.2.5**).

Taking into account such substituent effects, the author has now succeeded in the first syntheses of cellulose derivatives from both 3,6-di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate and 3-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate by cationic ring-opening polymerization.

After all, polymerization of **5** produced a cellulose derivative ($\overline{DP_n}$ = 19.3) with $[\alpha]_D$ value of -37.2° under optimum conditions. The cellulose derivative (Poly (**5**)) was converted into cellulose *via* cellulose triacetate with $[\alpha]_D$ value of -24.8°, which was further converted to cellulose having cellulose-II crystal structure (Section **4.3**). This instance is the first successful chemical entry into fully synthetic cellulose.

Finally, in the present studies, it was found that the 3-*O*-benzyl group has a special function for yielding a stereoregular polysaccharide not only in polymerizations of 1,4-anhydro-α-D-glucopyranose derivatives but also in those of α-D-glucopyranose 1,2,4-orthopivalate derivatives.

EXPERIMENTAL SECTION

Chapter 1

General. All melting points (mp) are uncorrected. ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded with a Varian XL-200 FT-NMR (200 MHz) spectrometer and a JEOL FX-90 FT-NMR (22.5 MHz), respectively, in chloroform-*d* with tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) and coupling constants (*J*) are given in δ-values (ppm) and Hz, respectively. Some chemical shift assignments were made using a decoupling method; others were made by an analogy with values in the literature and by analogy with model compounds. Optical rotations were measured using a JASCO Dip-4 digital polarimeter. UV (ultraviolet) spectra were recorded with a Shimadzu UV-365 spectrophotometer. IR (infrared) spectra were recorded with a Shimadzu FTIR-4000 spectrophotometer. Anhydrous dichloromethane was distilled from P_2O_5. Anhydrous tetrahydrofuran was distilled from potassium metal. Preparative thin layer chromatography (PTLC) was performed on silica-gel plates (Kieselgel 60 F_{254}, Merck). The standard work-up procedure included diluting with an ethyl acetate, washing with aq. $NaHCO_3$, and a brine, drying over Na_2SO_4, and evaporating *in vacuo*.

Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (10). *p*-Toluenesulfonic acid (3.3 g, 19 mM) was added to a solution of methyl α-D-glucopyranoside (**9**) (51.28 g, 0.2643 M) and benzaldehyde dimethylacetal (50 mL, 0.317 M) in *N*, *N*-dimethylformamide (DMF) (200 mL). The solution was kept at 40°C under 15 mmHg for 1 h. Solid $NaHCO_3$ (3.2 g) was added to the mixture. The solution was concentrated to a syrup. This syrup was worked-up by the standard procedure. Compound **10** was crystallized from EtOH (68 g , 91% yield), mp 163-165 °C, $[\alpha]_D^{32}$ + 108° (*c* (about) 0.67, chloroform), UV λ_{max} nm (ε) (dioxane): 250 (220), 255 (232), 261 (179), IR ν_{max} cm^{-1} (KBr) 3380 (OH), ^{1}H-NMR ($CDCl_3$): δ 3.43 (3 H (protons), OCH_3), 3.46 (t (triplet), 1 H, $J_{4,5}$ = 9, C_4-H), 3.59 (dd (double doublet), 3 H, $J_{2,3}$ = 9, C_2-H) 3.91 (t , 1 H, $J_{3,4}$ = 9,

C_3-H), 4.75 (d (doublet), 1 H, $J_{1,2}$ = 4, C_1-H) 5.50 (s (singlet), 1H, -C<u>H</u>C_6H_5) 7.34-7.54 (5 H, aromatic); [53] mp 164-165 °C, $[\alpha]_D$ + 117.5° (*c* 1, chloroform).

Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (11). Compound **10** (68 g , 0.241 M)was dissolved in DMF (300 mL). Sodium hydride (25 g , 0.627 M , 60% in mineral oil) and tetra-*n*-butyl ammonium iodide (0.9 g , 2.41 mM) were added and then benzyl bromide (74.5 mM , 0.627 mM) was added slowly dropwise at 0 °C with stirring. After 1 h, methanol (23 mL) was added to the reaction mixture for the decomposition of excess benzyl bromide. The reaction mixture was worked-up by the standard method. Compound **11** was crystallized from *n*-hexane (87 g, 78% yield), mp 95-96 °C, $[\alpha]_D^{32}$ - 21.0° (*c* 0.67, chloroform), UV λ_{max} nm (ε) (dioxane): 257 (536), ^{1}H-NMR ($CDCl_3$): δ 3.39 (3 H, OCH_3), 3.55 (dd, 1 H, $J_{2,3}$ = 9, C_2-H), 3.59 (t, 1 H, $J_{4,5}$ = 9, C_4-H), 4.04 (t, 1 H, $J_{3,4}$ = 9, C_3-H), 4.58 (d, 1 H, $J_{1,2}$ = 4, C_1-H), 5.55 (s, 1 H, -C<u>H</u>C_6H_5), 4.69, 4.82, 4.85, 4.94 (d, 4 H, C<u>H</u>$_2C_6H_5$), 7.26-7.60 (15 H, aromatic).

Anal. Calc. for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.60; H, 6.43.

1,4,6-Tri-*O*-acetyl-*O*-acetyl-2,3-di-*O*-benzyl-α-D-glucopyranoside (12) and 2,3-di-*O*-benzyl-D-glucopyranose (13). Compound **11** (46.2 g, 0.1 M) was dissolved in acetic anhydride (170 mL). Sulfuric acid (0.4 mL) in acetic anhydride (10 mL) was added dropwise to the solution at room temperature. For the completion of the reaction, an additional H_2SO_4/Ac_2O (1/25, v/v) solution (15.6 mL) was necessary. After 49 h, the reaction mixture was worked-up by the standard method and concentrated to as syrup **12** (*ca.* 48 g) which was used for the subsequent reaction without further purification. A small amount of this syrup was purified for the structural determination by crystallization from EtOH to afford compound **6** as colorless crystals, mp 117-120 °C, $[\alpha]_D^{32}$ + 38.2° (*c* 0.68, chloroform), UV λ_{max} nm (ε) (dioxane): 252 (311), 258 (378), 263 (297), IR.ν_{max} cm^{-1} (KBr): 1744 (C=O), 1226, 1254 (C-O), ^{1}H-NMR ($CDCl_3$): δ 1.95, 2.08, 2.20(9 H, Ac), 3.73 (dd, 1 H, $J_{2,3}$ = 9, C_2-H), 3.88 (t, 1 H, $J_{3,4}$ = 9, C_3-H), 4.00 (dd, 1 H, J = 2.5, J = 12, C_6-H), 4.23(dd, 1 H, J = 4.8, J = 12, C_6-H), 5.08 (dd, 1 H, $J_{4,5}$ = 9.5, C_4-H), 6.31 (d, 1 H, $J_{1,2}$ = 3.5, C_1-H), 7.30-7.34 (10 H, aromatic).

Anal. Calc. for $C_{26}H_{30}O_9$: C, 64.18; H, 6.22. Found: C, 64.01; H, 6.20.

The syrup **12** (*ca.* 48 g) was dissolved in MeOH / CH_2Cl_2 (100 mL, 1:4, v/v) and 28%-NaOMe in MeOH (40 mL) was added dropwise to the solution over a period of 20 min. After 3 h, the reaction mixture was treated with Amberlyst 15 ion-exchange resin for neutralization, and then the resin was filtered off. The filtrate was concentrated to dryness. The product was purified on a silica gel column (Wacogel C-200), eluted with CH_2Cl_2 to give a colorless oil (25.5 g, 70% yield (from compound **11**)). Compound **13** was crystallized from CH_2Cl_2, mp 113-116 °C, $[\alpha]_D^{32}$ + 51.0° (*c* 1, CH_3OH), UV λ_{max} nm (ε) (dioxane): 252 (311), 258 (318), 263 (251), IR ν_{max} cm^{-1} (KBr): 3440 (OH), ^{1}H-NMR ($CDCl_3$): δ 5.21 (d, $J_{1,2}$ = 3.5, C_1-H_a).

Anal. Calc. for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.43; H, 6.93.

2,3-Di-*O*-benzyl-6-*O*-pivaloyl-D-glucopyranose (14). To a solution of compound **13** (1.27 g , 3.53 mM) in pyridine (5 mL) pivaloyl chloride (0.80 mL , 6.67 mM) was added. After 1 min, the reaction mixture was diluted with ethyl acetate and washed successively with a saturated sodium hydrogencarbonate solution, aqueous hydrochloric acid, and brine. The organic phase was dried over Na_2SO_4 and concentrated to dryness. Compound **14** was crystallized from *n*-hexane (1.23 g, 79%), mp 115 °C, $[\alpha]_D^{32}$ + 16.5° (*c* 0.67, chloroform), UV λ_{max} nm (ε) (dioxane): 252 (336), 258 (400), 263 (314), IR ν_{max} cm^{-1} (KBr): 1716, 1732, 148 (C=O), 1284 (C-O), 3360 (OH), ^{1}H-NMR ($CDCl_3$): 3.80 (t, 1 H, *J* = 9, 9, C_3-H), 5.205 (d, $J_{1,2}$ = 3.5, C_1-H_a).

Anal. Calc. for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26. Found: C, 67.30; H, 7.21.

2,3-Di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranosyl dibenzyl phosphate (15). Crystalline **14** (0.474 g, 1.07 mL) was dried over P_2O_5 in a vacuum desiccator before use. *n*-Butyllithium (1.17 mM) was added to a solution of compound **14** in anhydrous tetrahydrofuran (15 mL) cooled below - 70 °C. After 30 min, dibenzyl phosphorochloridate (0.243 mL, 1.17 mM) was added to the solution. The reaction mixture was worked-up after 30 min by the standard procedure to yield a yellow syrup. Compound **15** was purified by PTLC (1:4, v/v, ethyl acetate/*n*-hexane) to give a

colorless syrup. (yield, 0.573 g, 79%),$[\alpha]^{22}$ + 48.4° (*c* 3.16, chloroform), UV λ_{max} nm (ε) (dioxane):261 (1440), 267 (1034), IR ν_{max} cm^{-1} (KBr): 1734 (C=O), 3440 (OH), 966, 1289 (P=O), ^{1}H-NMR ($CDCl_3$): δ 1.16 (9 H, C(C<u>H</u>$_3$)$_3$) , 3.44 (dd, 1 H, $J_{4,5}$ = 10, C_4-H), 3.55 (m, 1 H, $J_{2,3}$ = 9.0, $J_{2,P}$ = 3.0, C_2-H), 3.65-3.80 (m, 1 H, C_5-H), 3.71 (t, 1 H, $J_{3,4}$ = 9.0, C_3-H), 3.94 (dd, 1 H, $J_{6a,5}$ = 2.0, J_{gem} = 12.5, C_{6a}-H), 4.28 (dd, 1 H, $J_{6b,5}$ = 3.5, C_{6b}-H), 6.05 (dd, 1 H, $J_{1,2}$ = 3.0, $J_{1,P}$ = 7.0, C_1-H), 7.2-7.4 (20 H, aromatic).

1,4-Anhydro-2,3-di-*O*-benzyl-6-*O*-pivaloyl-α-D-glucopyranose (1). Compound **15** was dried over P_2O_5 below 0°C *in vacuo*. To a solution of compound **15** (324.5 mg, 0.480 mM) in anhydrous dichloromethane (20 mL) was added TMSOTf (9.2 μL ,0.048 mM) at 0 °C. The reaction mixture was worked-up after 1.5 h by the standard procedure. Compound **1** was purified by PTLC (1:4, v/v, ethyl acetate/*n*-hexane) to afford a colorless syrup (yield, 116.1 mg, 56.8%), $[\alpha]_D^{24}$ - 27.8° (*c* 0.65, chloroform), UV λ_{max} nm (ε) (dioxane): 252 (332), 258 (401), 263 (326), IR ν_{max} cm^{-1} (KBr): 1728 (C=O), ^{1}H-NMR ($CDCl_3$): δ 1.2 (9 H, C(C<u>H</u>$_3$)$_3$) , 3.70 (d, 1 H, $J_{2,3}$ = 2.5, C_2-H), 4.05 (dd, 1 H, $J_{3,4}$ = 5, C_3-H), 4.0-4.1 (m, 1 H, C_5-H), 4.47 (d, 1 H, *J* = 10, C_6-H), 4.55 (d, 1 H, *J* = 10, C_6-H), 4.655 (dd, 1 H, C_4-H), 5.455 (s, 1 H, $J_{1,2}$ = 0, C_1-H), 4.40, 4.45, 4.54, 4.55 (d, 4 H, *J* = 12, C<u>H</u>$_2$C$_6$H$_5$), ^{13}C-NMR ($CDCl_3$): δ 103.3 (C-1).

Anal. Calc. for $C_{25}H_{30}O_6$: C, 70.40; H, 7.09. Found: C, 70.41; H, 7.36.

3-*O*-Benzyl-4,6-*O*-benzylidene-D-glucopyranose (17). 3-*O*-Benzyl-D-glucopyranose(**16**) [17] (6.0 g, 22 mM) was treated as described for the synthesis of compound **10**, to give compound **11** (6.2 g, 17.3 mM). The crude product **17** was crystallized from *n*-hexane, mp 145-147 °C, $[\alpha]_D^{32}$ + 47.8° (*c* 0.69, chloroform), UV λ_{max} nm (ε) (dioxane): 257 (469), IR ν_{max} cm^{-1} (KBr): 3388 (OH), ^{1}H-NMR ($CDCl_3$): δ 3.51 (m, 1 H, C_5-H), 3.74 (dd, 1 H, $J_{2,3}$ = 9, C_2-H), 4.31 (dd, 1 H, *J* = 10.5, C_6-H), 5.325 (d, $J_{1,2}$ = 3.5, C_1-H_a), 4.76, 5.01 (d, *J* = 11, C<u>H</u>$_2$C$_6$H$_5$), 5.58 (s, 1 H, -C<u>H</u>C$_6$H$_5$) 7.22-7.6 (10 H, aromatic).

Anal. calc. for $C_{20}H_{22}O_60.5H_2O$: C,65.37;H,6.32. Found: C,65.18; H,6.35.

3-*O*-Benzyl-4,6-*O*-benzylidene-1,2-di-*O*-pivaloyl-β-D-glucopyranose (18). To a solution of compound **17** (1.547 g, 4.3 mM) in pyridine (10 mL) was added pivaloyl chloride (4.2 mL, 34.4 mM) at room temperature. The solution was kept at 80 °C for 5 h. The reaction mixture was worked-up in the same manner as described for the synthesis of compound **14**. The compound **18** was recrystallized from *n*-hexane (yield 1.85 g, 81.3%), mp 158-159 °C, $[\alpha]_D^{32}$ - 9.0° (*c* 0.67, chloroform), UV λ_{max} nm (ε) (dioxane): 257 (298), IR ν_{max} cm^{-1} (KBr): 1748, 1740 (C=O), 1276 (C-O), ^{1}H-NMR ($CDCl_3$): δ 1.10, 1.14 (18 H, C($C\underline{H}_3$)$_3$), 3.64 (m, C_5-H), 4.40 (dd, J = 10.5, 5, C_6-H), 5.225 (dd, 1 H, $J_{2,3}$ = 9, C_2-H), 5.72 (d, 1 H, $J_{1,2}$ = 8, C_1-H), 4.67, 4.89 (d, J = 11, $C\underline{H}_2C_6H_5$), 5.58 (s, 1 H, -$C\underline{H}C_6H_5$), 7.24-7.52 (10 H, aromatic).

Anal. Calc. for $C_{30}H_{22}O_8$: C, 68.42; H, 7.27. Found: C, 68.24; H, 7.38.

3,6-Di-*O*-benzyl-1,2-di-*O*-pivaloyl-β-D-glucopyranose (19). To a solution of compound **18** (1.052 g, 2 mM) in acetonitrile (10 mL) powdered molecular sieves 4Å (0.9 g) and sodium cyanoborohydride (0.53 g, 8 mM) were added. Trimethylchlorosilane (2.0 mL, 15.8 mM) was added dropwise over a period of 2 h to the reaction mixture. The reaction mixture was kept at room temperature for 3 h, filtered by use of Celite 535, and the residue was washed with ethyl acetate. The combined filtrate and washings was worked-up by the standard method to afford a yellow syrup. Compound **19** was purified on silica gel column (Wacogel C-200) eluted with dichloromethane to give colorless crystals (yield, 1.015 g, 96%), mp 47-48 °C, $[\alpha]_D^{32}$ + 7.5° (*c* 0.67, chloroform), UV λ_{max} nm (ε) (dioxane): 252 (470), 258 (528), 263 (442), IR ν_{max} cm^{-1} (KBr) 1744 (C=O), 3500 (OH), 1280 (C-O), ^{1}H-NMR ($CDCl_3$): δ 1.16, 1.20 (18 H, C($C\underline{H}_3$)$_3$), 3.62 (t, 1 H, $J_{3,4}$ = 9, C_3-H), 5.19 (dd, 1 H, $J_{2,3}$ = 9, C_2-H), 5.63 (d, 1 H, $J_{1,2}$ = 8, C_1-H), 7.3 (10 H, aromatic).

Anal. Calc. for $C_{30}H_{40}O_8$: C, 68.16; H, 7.63. Found: C, 67.88; H, 7.70.

3,6-Di-*O*-benzyl-2-*O*-pivaloyl-D-glucopyranose(20). To a solution of compound **19** (689 mg, 1.30 mM) in tetrahydrofuran (20 mL) was added hydrazine hydrate (*ca.* 90%, 254 μL, 4.69 mM) at room temperature. After 18 h, the reaction mixture was

worked-up by the standard method to give a colorless syrup. The product was purified by PTLC (1:2, v/v, ethyl acetate / *n*-hexane) to give colorless crystals **20** (yield, 0.427 mg, 73%), mp 43-44 °C, $[\alpha]_D^{32}$ + 36.0° (*c* 0.67, chloroform), UV λ_{max} nm (ε) (dioxane): 252 (509), 257 (493), 263 (314), IR ν_{max} cm^{-1} (KBr): 1288 (C-O), 1725 (C=O), 3400 (OH), ^{1}H-NMR ($CDCl_3$): δ 1.21 (9 H, C(C<u>H</u>$_3$)$_3$), 3.56 (t, 1 H , $J_{4,5}$ = 9, C_4-H), 3.6-3.75 (2H, C_6-H), 3.91 (dd, 1H, $J_{3,4}$ = 9, C_3-H), 4.03 (m, C_5-H), 4.75 (dd, 1 H, $J_{2,3}$ = 10.5, C_2-H), 5.385 (d, 1 H, $J_{1,2}$ = 3.5, C_1-H), 4.50, 4.57, 4.68, 4.84 (d, dd, d, d, 1 H, respectively, *J* = 11, C<u>H</u>$_2$C$_6$H$_5$), 7.3 (10 H, aromatic).

Anal. Calc. for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26. Found: C, 67.37; H, 7.37.

1,4-Anhydro-3,6-di-*O*-benzyl-2-*O*-pivaloyl-α-D-glucopyranose (2). Compound **20** (579.1 mg, 1.36 mM) was dissolved in benzene (500 mL), and then *p*-toluenesulfonic acid (23 mg, 0.136 mM) was added at reflux temperature. The solution was stirred at reflux temperature for 6.5 h with a Dean-Stark trap. The reaction mixture was worked-up by the standard procedure. Compound **2** was purified by PTLC (1:4, v/v, ethyl acetate/*n*-hexane) to afford colorless crystals (yield, 300.3 mg, 54.0%), mp 62.5-64.5 °C, $[\alpha]_D^{27}$ -20.9° (*c* 1.58, chloroform), UV λ_{max} nm (ε) (dioxane): 252 (245), 258 (274), 263 (240), IR ν_{max} cm^{-1} (KBr): 1722 (C=O), ^{1}H-NMR ($CDCl_3$): δ 1.2 (9 H, C(C<u>H</u>$_3$)$_3$), 3.86 (dd, 1 H, *J* = 10.5, 5, C_6-H), 3.96(d, 1 H, *J* = 10.5, C_6-H), 3.9-4.0 (m, 1 H, C_3-H), 4.16 (m, 1 H, C_5-H), 4.67 (dd, C_4-H), 4.78 (d, 1 H, $J_{2,3}$ = 2.5, C_2-H), 5.41 (s, 1 H, $J_{1,2}$ = 0, C_1-H), 4.46, 4.58, 4.59 (d, 2 H, 1 H, 1 H, respectively, C<u>H</u>$_2$C$_6$H$_5$), 7.32 (10 H, aromatic), ^{13}C-NMR ($CDCl_3$): δ 103.5 (C-1).

Anal. Calc. for $C_{25}H_{30}O_6$: C, 70.40; H, 7.09. Found: C, 70.13; H, 6.96.

3-*O*-Benzyl-1,2-di-*O*-pivaloyl-β-D-glucopyranose (21). To a suspension of 3-*O*-benzyl-4,6-*O*-benzylidene-1,2-di-*O*-pivaloyl-β-D-glucopyranose (**18**) [24] (2.57 g, 4.89 mM) in methanol (20 mL) was added *p*-toluenesulfonic acid (420 mg, 2.45 mM) at room temperature. After 3 h, the suspension turned to a clear solution. Solid $NaHCO_3$ was added to the mixture. The solution was concentrated to a syrup. The syrup was worked-up by the standard procedure. Compound **21** was crystallized from *n*-hexane (1.85 g, 86% yield), mp 100 - 102 °C, $[\alpha]_D$ -8.0° (*c* 0.95, chloroform), ^{1}H-NMR ($CDCl_3$):

δ 1.23-1.14 (18 H, piv-H), 3.50 (m, 1H, C_5-H), 3.34-3.90 (m, 2H, C_6-H), 3.65 (t, 1H, $J_{3,4}$ = 8, C_3-H), 3.76 (t, 1H, $J_{4,5}$ = 8, C_4-H), 4.64, 4.79 (d, 2H, J = 12, C<u>H</u>C_6H_5), 5.18 (t, 1H, $J_{2,3}$ = 8, C_2-H), 5.67 (d, 1H, $J_{1,2}$ = 8, C_1-H), 7.25-7.35 (5H, aromatic).

3-*O*-Benzyl-1,2,6-tri-*O*-pivaloyl-β-D-glucopyranose (22). To a solution of **21** (1.85 g, 4.22 mM) in pyridine (10 mL) was added pivaloyl chloride (0.78 mL, 6.34 mM) at room temperature. After 3 h, the reaction mixture was diluted with ethyl acetate and washed successively with a saturated sodium hydrogencarbonate solution, aqueous hydrochloric acid, and brine. The organic phase was dried over Na_2SO_4 and concentrated to dryness. 3-*O*-Benzyl-1,2,6-tri-*O*-pivaloyl-β-D-glucopyranose (**22**) was crystallized from *n*-hexane (1.92 g, 87% yield), mp 116 - 119 °C, $[\alpha]_D$ -11.5° (*c* 0.93, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.17-1.20 (27H, piv-H), 3.50-3.65 (m, 3H, C_3-H, C_4-H, C_5-H), 4.27 (dd, 1H, J_{gem} = 12, $J_{5,6}$ = 1.9, C_6-H), 4.44 (dd, 1H, $J_{5,6'}$ = 4.5, $C_{6'}$-H), 4.70-4.74 (2H, C<u>H</u>$_2C_6H_5$), 5.14 (t, $J_{2,3}$ = 8, C_2-H), 5.62 (d, 1H, $J_{1,2}$ = 8, C_1-H), 7.28-7.35 (5H, aromatic).

3-*O*-Benzyl-2,6-di-*O*-pivaloyl-D-glucopyranose (23). To a solution of **22** (1.92 g, 3.68 mM) in 1,4-dioxane (22 mL) was added hydrazine hydrate (*ca.* 90%, 357 μL, 7.36 mM) at 50°C. After 15 h, the reaction mixture was worked-up by the standard method to give a colorless syrup. The product was purified by PTLC (1:2, v/v, ethyl acetate/*n*-hexane) to give colorless crystals **23** (1.24 g, 77% yield), mp 45 - 50 °C, $[\alpha]_D$ +38.6° (*c* 1.09, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.16-1.28 (18H, piv-H), 7.26-7.35 (5H, aromatic).

1,4-Anhydro-3-*O*-benzyl-2,6-di-*O*-pivaloyl-α-D-glucopyranose (3). To a solution of **23** (436.9 mg, 1.00 mM) in benzene (450 mL) was added *p*-toluenesulfonic acid (17 mg, 0.1 mM). The solution was stirred at reflux temperature for 23 h with a Dean-Stark trap. The reaction mixture was worked-up by the standard procedure. Compound **3** was purified by PTLC (1:4, v/v, ethyl acetate/*n*-hexane) to afford colorless crystals (193.1 mg, 46% yield), mp 81 - 82 °C, $[\alpha]_D$ -0.2° (*c* 1.15, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.20 (18H, piv-H), 3.97 (m, 1H, $J_{3,4}$ = 5, C_3-H), 4.09 (m, 1H, C_5-H), 4.45 (d, 1H, J_{gem} = 12, C_6-H), 4.59 (dd, 1H, $J_{5,6'}$ = 3.5, $C_{6'}$-H), 4.50, 4.67 (d, 1H, J

= 12, C<u>H</u>C_6H_5, respectively) 4.68 (dd, 1H, $J_{4,5}$ = 3, C_4-H), 4.80 (d, 1H, $J_{2,3}$ = 2.5, C_2-H), 5.43 (s, 1H, $J_{1,2}$ = 0, C_1-H), 7.2-7.3 (5H, aromatic).

4,6-*O*-Benzylidene-D-glucopyranose (25). To a suspension of D-glucopyranose (**24**) (18 g, 100 mM) in *N,N'*-dimethylformamide (18 mL) was added benzaldehyde dimethylacetal (18 mL, 120 mM). The solution was kept at 50°C under 15 mmHg for 40 min. Solid $NaHCO_3$ was added to the mixture. The solution was concentrated to a syrup. The reaction mixture was diluted with water, and washed with dichloromethane. The water layer was concentrated to dryness, yielding compound **25** as a syrup which was crystallized from water, obtained by filtration, washed with water, and dried by heating (80°C, 8 h) (7.5 g, 28% yield), mp 172 - 173 °C, $[\alpha]_D$ -3.3° (*c* 0.89, methanol), ^{1}H-NMR ($CDCl_3$): δ 5.55 (s, 1H, C<u>H</u>C_6H_5), 7.37 - 7.50 (5H, aromatic).

4,6-*O*-Benzylidene-1,2,3-tri-*O*-pivaloyl-β-D-glucopyranose (26). To a solution of **25** (7.5 g, 28 mM) in pyridine (20 mL) was added pivaloyl chloride (15.5 mL, 127 mM) at 80°C. After 12 h, the reaction mixture was diluted with ethyl acetate and washed successively with a saturated sodium hydrogencarbonate solution, aqueous hydrochloric acid, and brine. The organic phase was dried over Na_2SO_4 and concentrated to dryness. Compound **26** was crystallized from *n*-hexane to afford colorless crystals (11.1 g, 76% yield), mp 152 - 153 °C, $[\alpha]_D$ -43.9° (*c* 3.03, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.12-1.19 (27H, piv-H), 3.60-3.82 (m, 3H, C_4-H, C_6-H, $C_{6'}$-H), 4.41 (dd, 1H, *J* = 10.9, 6.4, C_5-H), 5.24 (dd, 1H, $J_{2,3}$ = 9, C_2-H), 5.42 (d, $J_{3,4}$ = 9.4, C_3-H), 5.52 (s, 1H, C<u>H</u>C_6H_5), 5.79 (d, 1H, $J_{1,2}$ = 8, C_1-H) 7.33-7.41 (5H, aromatic).

6-*O*-Benzyl-1,2,3-tri-*O*-pivaloyl-β-D-glucopyranose (27). To a solution of **26** (1.04 g, 2.0 mM) in acetonitrile (10 mL), powdered molecular sieves 4Å (1.0 g) and $NaHCO_3$ (0.53 g, 8.0 mM) were added. Trimethylchlorosilane (2.0 mL, 15.8 mM) was added dropwise over a period of 1.5 h to the reaction mixture. The reaction mixture was filtered using Celite 535, and the residue was washed with ethyl acetate. The combined filtrate and washings were worked-up by the standard method to afford a yellow syrup. Compound **27** was purified on a silica gel column (Wacogel C-200) eluted

with dichloromethane to give colorless crystals (1.04 g, *ca.* 100%), mp 85.4-88 °C $[\alpha]_D$ -5.8° (*c* 1.44, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.10-1.19 (27H, piv-H), 3.64-3.84 (m, 4H, C_4-H, C_5-H, C_6-H, $C_{6'}$-H), 4.61, 4.53 (d, d, 1H, *J* = 12, respectively, $C\underline{H}_2C_6H_5$), 7.29-7.33 (5H, aromatic).

6-*O*-Benzyl-2,3-di-*O*-pivaloyl-D-glucopyranose (28). To a solution of **27** (303 mg, 0.580 mM) in THF (8 mL) was added hydrazine hydrate (*ca.* 90%, 112 μL, 2.32 mM) at 50°C. After 51 h, the reaction mixture was worked-up by the standard method to give a colorless syrup. Compound **28** was purified by PTLC (1:2, v/v, ethyl acetate/*n*-hexane) to afford a colorless syrup (189 mg, 74% yield), $[\alpha]_D$ +46.7° (*c* 1.05, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.19-1.20 (18H, piv-H), 4.58 (2H, $C\underline{H}_2C_6H_5$), 7.26-7.35 (5H, aromatic).

1,4-Anhydro-6-*O*-benzyl-2,3-di-*O*-pivaloyl-α-D-glucopyranose (4). To a solution of **28** (386 mg, 0.880 mM) in benzene (500 mL) was added *p*-toluenesulfonic acid (15.2 mg, 0.088 mM) at reflux temperature. The solution was stirred at reflux temperature for 51 h with a Dean-Stark trap. The reaction mixture was worked-up by the standard procedure. Compound **4** was purified by PTLC (1:4, v/v, ethyl acetate/*n*-hexane) to give colorless crystals (234 mg, 63% yield), mp 42.4 - 43.9 °C, $[\alpha]_D$ -9.5° (*c* 1.34, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.12-1.20 (18H, piv-H), 3.70 (dd, 1H, J_{gem} = 11, $J_{5,6}$ = 3.5, C_6-H), 3.82 (dd, 1H, $J_{5,6'}$ = 8, C_6-H) 4.19 (m, 1H, C_5-H), 4.54, 4.65 (d, d, 1H, respectively, $C\underline{H}_2C_6H_5$), 4.74 (d, 1H, $J_{2,3}$ = 2.5, C_2-H), 4.81 (dd, 1H, $J_{4,5}$ = 3, C_4-H), 5.46 (s, 1H, $J_{1,2}$ = 0, C_1-H), 7.32 (5H, aromatic), ^{13}C-NMR: δ 103.3 (C-1).

Chapter 2

Polymerization. All polymerizations were carried out using a high vacuum line capable of maintaining a vacuum of 1 x 10^{-3} Torr (Figure 17). Monomer was dried in a polymerization ampule by evacuating for a few hours. Methylene chloride was dried over P_2O_5, distilled, and degassed by freezing and thawing three times in a high vacuum line. All solvents were transferred under high vacuum. Phosphorus pentafluoride was generated from *p*-chlorobenzenediazonium hexafluorophosphate by

decomposition at 160 °C and transferred to a reaction ampule. $SbCl_5$, $BF_3 \bullet Et_2O$ and $(CF_3SO_2)_2O$ were added into the reaction ampule through the rubber septum by syringe. The reaction apparatus was then separated by melting at a constriction and placed in a bath of the appropriate temperature. Polymerizations were terminated by adding cold methanol at the polymerization temperature. After dilution with ethyl acetate and chloroform (v/v, 1:1), the polymer solution was washed with water. The solution was dried over anhydrous sodium sulfate and concentrated to dryness. *n*-Hexane was added to the polymer mixture. The remaining monomer was repeatedly extracted with hot *n*-hexane while applying ultrasonic waves. The residual polymer was finally dried *in vacuo*.

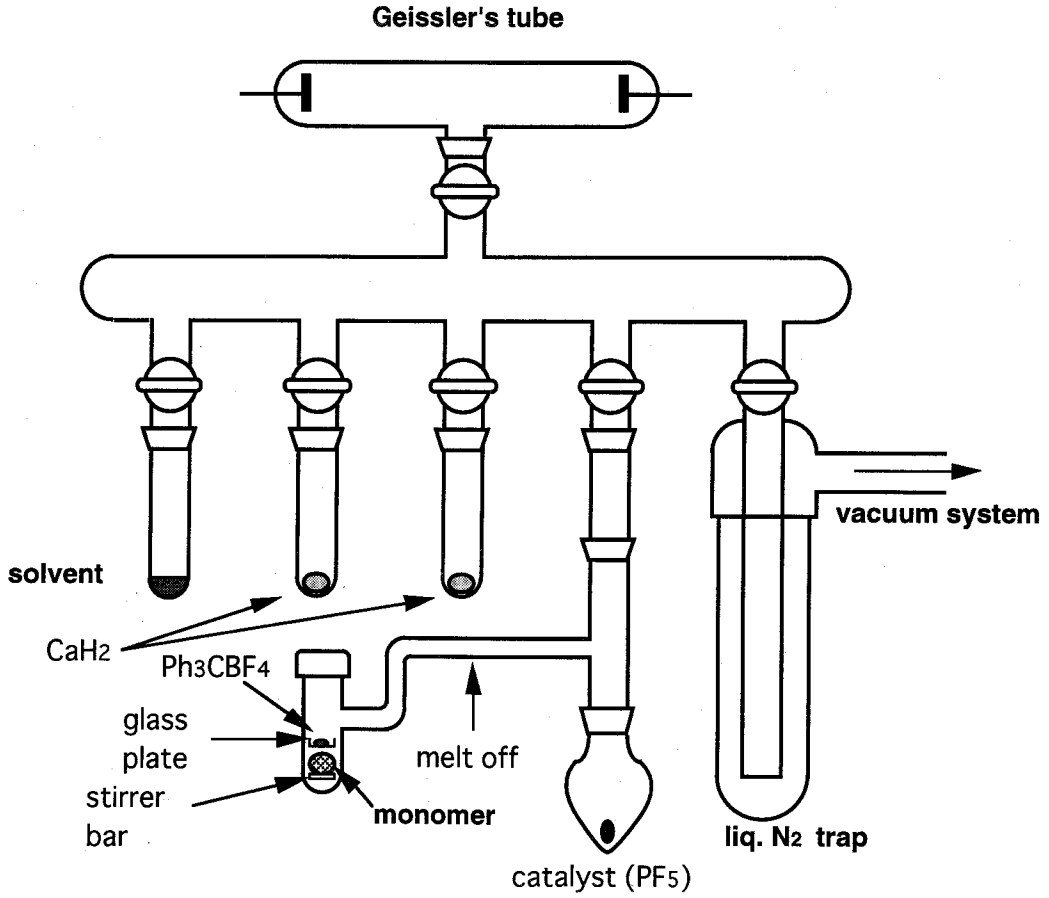


Figure 17 Vacuum line.

Deprotection. The stereoregular (1→5)-β-D-glucofuranan derivative (25.6 mg) was dissolved in toluene (0.2 mL) and 1,2-dimethoxyethane (0.2 mL) was added

dropwise to a solution of small pieces of metal sodium in 5 mL of liquid ammonia at -78 °C. The reaction was allowed to continue for 2 h, followed by successive addition of ammonium chloride and several drops of water. Deprotected polymer was dialyzed with water, and freeze-dried (yield, 4.5 mg, 46%). $[\alpha]_D$ (*c* 0.1, H_2O) = -204°, ^{13}C-NMR (D_2O, DSS as external standard): δ 108.0 (C-1), 82.8, 82.2, 77.4, 75.8 (C-2, C-3, C-4, C-5), 61.5 (C-6). Selected polymers were deprotected by the above-mentioned method.

Acetylation of Deprotected Polymer. The deprotected polymer was acetylated by acetic anhydride / pyridine (3 : 1, v/v) at 60 °C. After 12 h, the reaction mixture was concentrated to dryness. The acetylated (1→5)-β-D-glucofuranan had $[\alpha]_D$ -76.8° (*c* 0.95, $CHCl_3$); ^{13}C-NMR ($CDCl_3$): δ 106.2 (C-1), 79.9, 79.2, 73.7 (C-2, C-3, C-4, C-5), 62.2 (C-6), 170.6, 169.9, 169.0 (C=O), 20.7 (Ac). Selected polymers were acetylated by the above-mentioned method.

Measurements. The 200-MHz ^{1}H-NMR and the 22.5-MHz ^{13}C-NMR spectra of substituted glucans were measured in $CDCl_3$ at ambient temperature with tetramethylsilane (TMS) as the internal standard using a Varian XL-200 FT-NMR spectrometer and a JEOL FX-90Q FT-NMR spectrometer, respectively. The chemical shifts are expressed in ppm downfield of the internal TMS absorption. The ^{13}C-NMR spectrum of unsubstitiuted glucan was recorded in D_2O with DSS (sodium 2,2-dimethyl-2-silapentane-5-sulfonate) as external standard. The structure of selected stereoregular (1→5)-β-D-glucofuranan derivative was established using two-dimensional homo- and heteronuclear NMR experiments using a Brucker AM-500. Specific rotations were measured with a JASCO Dip-4 digital polarimeter in $CHCl_3$ or H_2O at 25 °C. Infrared spectra were recorded with a Shimazu FT IR-4000 spectrophotometer. Molecular weight distributions of the substituted polymer were analyzed by gel permeation chromatography in tetrahydrofuran. A Waters universal liquid chromatograph injector (model U6K), a Waters solvent delivery system (model 6000A), a Waters refractive index detector (series R-400), a Waters absorbance detector (model 440), and Shodex columns (KF802 and KF803) were used. The flow

rate was 1.0 mL/min. Calibration curves were obtained by using polystyrene standards (Shodex).

Chapter 3

General Methods. Anhydrous dichloromethane was distilled from P_2O_5. Preparative thin layer chromatography (PTLC) was performed on silica-gel plates (Kieselgel 60 F_{254}, Merck). The standard work-up procedure included diluting with ethyl acetate, washing with aq. $NaHCO_3$, and brine, drying over Na_2SO_4, and evaporating *in vacuo*.

Measurements. All melting points (mp) are uncorrected. ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded with a Bruker AC300 FT-NMR (300 MHz) spectrometer and a JEOL FX-90 FT-NMR (22.5 MHz), respectively, in chloroform-*d* with tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) and coupling constants (*J*) are given in δ-values (ppm) and Hz, respectively. Some chemical shift assignments were made using a decoupling method; others were made by an analogy with values in the literature and by analogy with model compounds. Optical rotations were measured using a JASCO Dip-1000 digital polarimeter.

3,6-Di-*O*-benzyl-α-D-glucopyranose 1,2,4-orthopivalate (5). 3,6-Di-*O*-benzyl-2-*O*-pivaloyl-D-glucopyranose (**20**) [24] (298.7 mg, 0.67 mM) was dissolved in benzene (40 mL), and then *N, N'*-carbonyldiimidazole (116.9 mg, 1.05 eq.) was added. The solution was stirred at reflux temperature for 31 h. The reaction mixture was concentrated *in vacuo*. Compound **5** was purified on silica gel column (Wacogel C-200) eluted with ethyl acetate / *n*-hexane (1 / 4, v / v) to give colorless crystals (180 mg, 62.8 %), mp 58.7-59.2 °C (recrystallized from methanol), $[\alpha]_D$ +22.1° (*c* 1, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.05 (9H, piv-H), 3.75 (dd, 1H, J_{gem} = 9.6, $J_{5,\,6a}$ = 7.1, C_6-H_a), 3.83 (dd, 1H, J_{gem} = 9.6, $J_{5,\,6b}$ = 7.1, C_6-H_b), 3.95 (collapsed dt, 1H, $J_{2,\,4}$ = 2.0, $J_{3,\,4}$ = 4.6, $J_{4,\,5}$ = 1.4, C_4-H), 4.31 (dd, 1H, $J_{2,\,3}$ = 2.0, $J_{3,\,4}$ = 4.6, C_3-H), 4.42 (dt, 1H, $J_{1,\,2}$ = 4.9, $J_{2,\,3}$ = $J_{2,\,4}$ = 2.0, C_2-H), 4.60 (collapsed t, 1H, $J_{4,\,5}$ = 1.4, $J_{5,\,6a}$ = $J_{5,\,6b}$ = 7.1, C_5-H), 5.79 (d, 1H, $J_{1,\,2}$ = 4.9, C_1-H), 4.50, 4.55 5.65 (d, s, d, 1H, 2H, 1H, respectively, *J* =

12.0, $C\underline{H}_2C_6H_5$), 7.09-7.26 (10H, aromatic), ^{13}C-NMR: δ 97.6 (C-1), 75.8, 73.4, 72.3, 71.9, 71.7, 71.2, 70.1 (C-2, C-3, C-3, C-4, C-5, C-6, $\underline{C}H_2C_6H_5$), 123.1 ($\underline{C}(CH_3)_3$), 24.9 ($C(\underline{C}H_3)_3$).

Anal. ($C_{25}H_{30}O_6$): calcd, C, 70.40; H, 7.09; found, C, 70.27; H, 7.06.

3-*O*-Benzyl-6-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (6). 3-*O*-Benzyl-2,6-di-*O*-pivaloyl-D-glucopyranose (**23**) [25] (576 mg, 1.32 mM) was dissolved in benzene (50 mL), and then *N, N'*-carbonyldiimidazole (228 mg, 1.05 eq.) was added. The solution was stirred at reflux temperature for 5 days. The reaction mixture was concentrated *in vacuo*. Compound **6** was purified on silica gel column (Wacogel C-200) eluted with ethyl acetate / *n*-hexane (1 / 4, v / v) to give colorless crystals (318 mg, 57.6 %), mp 73.1 - 73.6 °C (recrystallized from methanol), $[\alpha]_D$ +31.2° (*c* 1.35, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.03 (9H, piv-H), 1.23 (9H, piv-H), 3.95 (dt, 1H, $J_{4,5}$ = 1.1, C_4-H), 4.16 (dd, 1H, $J_{2,3}$ = 2.2, $J_{3,4}$ = 4.7, C_3-H), 4.31-4.41 (2H, C_6-H), 4.39-4.43 (1H, C_2-H), 4.45-4.52 (1H, C_5-H), 5.76 (d, 1H, $J_{1,2}$ = 4.9, C_1-H), 4.63 (s, 2H, J = 12.0, $C\underline{H}_2C_6H_5$), 7.30-7.40 (5H, aromatic), ^{13}C-NMR: δ 97.6 (C-1), 64.4, 71.3, 71.5, 72.0, 72.2, 75.3 (C-2, C-3, C-3, C-4, C-5, C-6, $\underline{C}H_2C_6H_5$), 123.1 ($(\text{-O})_3\underline{C}(CH_3)_3$), 27.2 (pivaloyl-$C(\underline{C}H_3)_3$), 38.8 (pivaloyl-$\underline{C}(CH_3)_3$), 24.9 (orthopivalate-$C(\underline{C}H_3)_3$), 35.7 (orthopivalate-$\underline{C}(CH_3)_3$), 127.7, 128.1, 128.7, 137.4 (aromatic).

6-*O*-Benzyl-3-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (7). 6-*O*-Benzyl-2,3-di-*O*-pivaloyl-D-glucopyranose (**28**) [25] (307.8 mg, 0.703 mM) was dissolved in benzene (50 mL), and then *N, N'*-carbonyldiimidazole (120 mg, 1.05 eq.) was added. The solution was stirred at reflux temperature for a week. The reaction mixture was concentrated *in vacuo*. Compound **7** was purified on silica gel column (Wacogel C-200) eluted with ethyl acetate / *n*-hexane (1 / 4, v / v) to give colorless crystals (103.7 mg, 35.1 %), mp 85.9-86.9 °C (recrystallized from methanol), $[\alpha]_D$ +10.1° (*c* 1.07, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.06 (9H, piv-H), 1.11 (9H, piv-H), 3.61 (dd, 1H, J_{gem} = 9.6, $J_{5,6a}$ = 6.5, C_6-H_a), 3.72 (dd, 1H, $J_{5,6b}$ = 6.5, C_6-H_b), 4.31 (dd, 1H, $J_{2,3}$ = 2.2, $J_{3,4}$ = 4.7, C_3-H), 4.38 (m, 1H, C_2-H), 4.62 (t, 1H, C_5-H), 5.08 (dt, 1H, $J_{4,5}$ = 1.1, C_4-H), 5.73 (d, 1H, $J_{1,2}$ = 4.8, C_1-H), 4.51, 4.60 (d, d, 1H, 1H, respectively, J = 12.0,

$C\underline{H}_2C_6H_5$), 7.20-7.40 (5H, aromatic), ^{13}C-NMR: δ 97.4 (C-1), 65.7, 69.6, 70.7, 72.0, 73.3, 75.5 (C-2, C-3, C-3, C-4, C-5, C-6, $\underline{C}H_2C_6H_5$), 123.3 ((-O)$_3\underline{C}(CH_3)_3$), 27.0 (pivaloyl-C($\underline{C}H_3)_3$), 38.7 (pivaloyl-$\underline{C}(CH_3)_3$), 24.8 (orthopivalate-C($\underline{C}H_3)_3$), 35.7 (orthopivalate-$\underline{C}(CH_3)_3$), 127.7, 127.8, 128.4, 137.7 (aromatic).

1,2,3-Tri-*O*-pivaloyl-β-D-glucopyranose (29). To a suspension of 4,6-*O*-benzylidene-1,2,3-tri-*O*-pivaloyl-β-D-glucopyranose (**26**) [25] (1.04 g, 2.0 mM) in methanol (10 mL) was added *p*-toluenesulfonic acid (172 mg, 1.0 mM) at room temperature. After 2 h, the suspension turned to a clear solution. The solution was worked-up by the standard procedure. Compound **29** was crystallized from *n*-hexane (756 mg, 87% yield), mp 147.6 - 148.6 °C, $[\alpha]_D$ -1.7° (*c* 0.838, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.13, 1.186, 1.194 (9H, 9H, 9H, piv-H), 3.58 (m, 1H, C_5-H), 3.76-3.88 (m, 1H, C_4-H), 3.76-3.82 (1H, C_6-H_a), 3.91-3.98 (m, 1H, C_6-H_b), 5.10-5.20 (2H, C_2-H, C_3-H), 5.72 (d, 1H, $J_{1,2}$ = 8.1, C_1-H).

1,2,3,6-Tetra-*O*-pivaloyl-β-D-glucopyranose (30). To a solution of **6** (756 mg, 1.75 mM) in pyridine (5 mL) was added pivaloyl chloride (0.323 mL, 2.63 mM) at room temperature. After 1 h, the reaction mixture was diluted with ethyl acetate and washed successively with a saturated sodium hydrogencarbonate solution, aqueous hydrochloric acid, and brine. The organic phase was dried over Na_2SO_4 and concentrated to dryness. Compound **30** was crystallized from *n*-hexane (851 mg, 94% yield), mp 147.9 - 148.8 °C, $[\alpha]_D$ -12.4° (*c* 0.709, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.19, 1.20, 1.23 (9H, 9H, 9H, piv-H), 3.50 (m, 1H, C_4-H), 4.07 (m, 1H, C_5-H), 4.36 (dd, 1H, J_{gem} = 12.2, $J_{5,6a}$ = 2.6, C_6-H_a), 4.42 (dd, 1H, $J_{5,6b}$ = 4.0, C_6-H_b), 4.80 (d, 1H, $J_{1,2}$ = 10.1, J = 3.7, C_1-H), 5.40 (t, 1H, $J_{2,3}$ = 10.1, C_2-H), 5.45 (1H, C_3-H).

2,3,6-Tri-*O*-pivaloyl-D-glucopyranose (31). To a solution of **30** (696.4 mg, 1.35 mM) in THF (10 mL) was added hydrazine hydrate (*ca.* 90%, 131 μL, 2.8 mM) at room pemperature. After 8 h, the reaction mixture was worked-up by the standard method to give colorless syrup. Compound **31** was crystallized from *n*-hexane (478.8 mg, 82 % yield), mp 68.8 - 69.4 °C, $[\alpha]_D$ +65.1° (*c* 0.767, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.13, 1.17, 1.19, 1.22 (9H, 9H, 9H, 9H, piv-H), 3.50-3.57 (m, 1H, C_4-H), 3.64-3.70 (m, 1H,

C_5-H), 4.32 (dd, 1H, J_{gem} = 12.2, $J_{5,\ 6a}$ = 2.5, C_6-H_a), 4.45 (dd, 1H, $J_{5,\ 6b}$ = 4.7, C_6-H_b), 5.08-5.18 (2H, C_2-H, C_3-H), 5.68 (d, 1H, $J_{1,\ 2}$ = 8.1, C_1-H).

3,6-Di-*O*-pivaloyl-α-D-glucopyranose 1,2,4-orthopivalate (8) Compound **31** (44.9 mg, 0.104 mM) was dissolved in benzene (40 mL), and then *N, N'*-carbonyldiimidazole (116.9 mg, 1.05 eq.) was added. The solution was stirred at reflux temperature for 9 days The reaction mixture was concentrated *in vacuo*. Compound **8** was purified on silica gel column (Wacogel C-200) eluted with ethyl acetate / *n*-hexane (1 / 4, v / v) to give colorless crystals (19.7 mg, 45.8 %), mp 127.3 - 128.7 °C (recrystallized from methanol), $[\alpha]_D$ +20.5° (*c* 0.77, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.06, 1.22, 1.23 (9H, 9H, 9H, piv-H), 4.21 (dd, 1H, J_{gem} = 9.6, $J_{5,\ 6a}$ = 6.8, C_6-H_a), 4.25 (dd, 1H, $J_{2,\ 3}$ = 2.2, $J_{3,\ 4}$ = 4.7, C_3-H), 4.38 (dd, 1H, $J_{5,\ 6b}$ = 6.5, C_6-H_b), 4.43 (m, 1H, C_2-H), 4.56 (t, 1H, C_5-H), 5.12 (dt, 1H, $J_{4,\ 5}$ = 1.1, C_4-H), 5.75 (d, 1H, $J_{1,\ 2}$ = 4.8, C_1-H), ^{13}C-NMR: δ 97.4 (C-1), 63.8, 65.6, 70.8, 72.0, 74.9 (C-2, C-3, C-3, C-4, C-5, C-6), 123.5 ((-O)$_3$$\underline{C}$$(CH_3)_3$), 27.2 (pivaloyl-C($\underline{C}H_3)_3$), 38.8, 38.9 (pivaloyl-$\underline{C}$$(CH_3)_3$), 24.8 (orthopivalate-C($\underline{C}H_3)_3$), 35.8 (orthopivalate-$\underline{C}$$(CH_3)_3$).

Chapter 4

General Methods. Anhydrous dichloromethane was distilled from P_2O_5. Preparative thin layer chromatography (PTLC) was performed on silica-gel plates (Kieselgel 60 F_{254}, Merck). The standard work-up procedure included diluting with ethyl acetate, washing with aq. $NaHCO_3$, and brine, drying over Na_2SO_4, and evaporating *in vacuo*.

Polymerization of Compound 5.

All polymerizations were carried out using a high-vacuum line capable of maintaining a vacuum of 1×10^{-3} Torr (Figure 17). Monomer was dried in a polymerization ampule by evacuating for *ca.* a day. Methylene chloride was distilled from CaH_2, and degassed by freezing and thawing three times in a high-vacuum line. The solvent was transferred under high vacuum. Phosphorus pentafluoride was generated from *p*-chlorobenzenediazonium hexafluorophosphate by decomposition at

160 °C and transferred to a reaction ampule. BF_3•Et_2O was added into the reaction ampule through a rubber septum by syringe. Triphenylcarbenium tetrafluoroborate was placed on a small glass plate in the reaction ampule with compound **5**. The reaction apparatus was then separated by melting off and placed in a bath of the appropriate temperature. The reaction mixture was diluted with toluene/chloroform (1/1, v/v), washed with saturated aq. $NaHCO_3$, water, and brine, dried over anhydrous sodium sulfate, and concentrated to dryness. The polymer mixture was dissolved in a small amount of chloroform. To the solution, *n*-hexane was added, and then residual polymer, 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→4)-β-D-glucopyranan (poly(**5**)) was collected by filtration, and finally dried *in vacuo*, mp 206 - 217 °C, $[\alpha]_D$ -37.2° (*c* 0.65, chloroform), ^{1}H-NMR ($CDCl_3$): δ 0.97-1.13 (9H, piv-H), 3.04 (m, 1H, C_5-H), 3.16 (broad t, 1H, $J_{2,3}$ = 8.7, $J_{3,4}$ = 8.5, C_3-H), 3.48 (m, 2H, C_6-H), 3.97 (broad t, 1H, $J_{3,4}$ = 8.5, $J_{4,5}$ = 9.2, C_4-H), 4.23 (d, 1H, $J_{1,2}$ = 8.7, C_1-H), 4.95 (t, 1H, $J_{1,2} = J_{2,3}$ = 8.7, C_2-H), 3.85, 4.16-4.20, 4.35, 5.17 (d, 1H, J = 12.0, respectively, $C\underline{H}_2C_6H_5$), 7.07-7.24 (10H, aromatic), ^{13}C-NMR: δ 99.4 (C-1), 81.1 (C-4), 67.4 (C-6), 75.4, 74.8, 74.2, 73.3, 72.4 (C-2, C-3, C-3, C-5, $\underline{C}H_2C_6H_5$), 128.5, 128.2, 127.8, 126.5, 139.2, 137.7 (aromatic), 176.5 (C=O).

Preparation of Cellulose (34).

2,3,6-Tri-*O*-acetyl-(1→4)-β-D-glucopyranan (33). To a solution of 3,6-di-*O*-benzyl-2-*O*-pivaloyl-(1→4)-β-D-glucopyranan (poly(**5**)) (150.4 mg) in THF / methanol (10 / 1, v / v) (40 mL), 28%-sodium methoxide in methanol (1.5 mL) was added. The reaction mixture was kept at reflux temperature over night, treated with Amberlyst 15 ion-exchange resin for neutralization, and then filtered off. The resin was washed with chloroform. The combined washings and filtrate were concentrated to dryness. The product was treated with acetic anhydride and pyridine at 50 °C overnight to give 3,6-di-*O*-benzyl-2-*O*-acetyl-(1→4)-β-D-glucopyranan (**32**). To a solution of the compound **32** in THF / acetic acid (1 / 1, v / v) (5 mL), palladium hydroxide on carbon (180 mg) was added. The reaction mixture was kept under 4.5 kgf / cm^2 at room temperature for an hour. The reaction mixture was concentrated, and treated with acetic anhydride and pyridine at 50 °C overnight, and concentrated to dryness. The

product was washed with methanol and collected by filtration to give 2,3,6-tri-*O*-acetyl-(1→4)-β-D-glucopyranan (**33**) (69 mg, 68 % overall yield from poly(**5**)), mp 299 - 306 °C (dec.); $[\alpha]_D$ -24.8° (*c* 1.3, chloroform), ^{1}H-NMR ($CDCl_3$): δ 1.95, 2.03, 2.13 (C_3-Ac, C_2-Ac, C_6-Ac, 3H, 3H, 3H, respectively), 3.55 (m, 1H, C_5-H), 3.71 (t, 1H, $J_{3,4} = J_{4,5} = 9.3$, C_4-H), 4.06 (d, 1H, $J = 7.4$, C_6-H_a), 4.36-4.43 (2H, C_1-H, C_6-H_b), 4.79 (t, 1H, $J_{1,2} = J_{2,3} = 9.0$, C_2-H), 5.07 (t, 1H, $J_{2,3} = 9.0$, $J_{3,4} = 9.3$, C_3-H), ^{13}C-NMR: δ 100.5 (C-1), 72.0 (C-2), 72.6 (C-3), 76.2 (C-4), 73.0 (C-5), 62.1 (C-6), 20.8, 20.5 (Ac-C), 169.2, 169.7, 170.2 (C_2-C=O, C_3-C=O, C_6-C=O, respectively).

(1→4)-β-D-Glucopyranan, cellulose (34). To a solution of compound **33** (14.8 mg) in THF / methanol (10 / 1, v / v) (4.4 mL), 28%- sodium methoxide in methanol (0.15 mL) was added. The reaction mixture was kept at room temperature for 48 h, and neutralized with 1N-HCl. The precipitated polymer was centrifuged, washed with methanol, and collected by filtration to give (1→4)-β-D-glucopyranan, cellulose (**34**) (6.3 mg, 73 %).

Conversion of Poly(7) into Acetylated Poly(7).

To a solution of poly(**7**) (9.2 mg) (Table 10, experiment no. 7) in THF / methanol (10 / 1, v / v) (3.3 mL), 28%- sodium methoxide (0.1 mL) was added. The reaction mixture was kept at reflux temperature for 27 h. Then, MeOH (*ca.* 2 mL) was added to the reaction mixture. After 5 h, the reaction mixture was treated with Amberlyst 15 ion-exchange resin for neutralization, and then filtered off. The resin was washed with MeOH. The combined washings and filtrate were concentrated to dryness. The product was treated with acetic anhydride and pyridine at 50 °C overnight to give a crude 2,3-di-*O*-acetyl-6-*O*-benzyl derivative. The product was purified by silicagel column (Wacogel C-200; eluent: $CHCl_3$, and then 20% MeOH / $CHCl_3$), and by TLC (eluent: 10% MeOH / $CHCl_3$).give 2,3-di-*O*-acetyl-6-*O*-benzyl derivative (7.1 mg, 96%); ^{13}C-NMR: δ 100.2, 99.9, and 97.3 ppm (C_1 region). To a solution of the 2,3-di-*O*-acetyl-6-*O*-benzyl derivative (7.1 mg) in THF (1 mL), palladium hydroxide on carbon (40 mg) was added. The reaction mixture was kept at room temperature for about one day. Palladium hydroxide on carbon was filtered off, and washed with chloroform. The

combined washings and filtrate were concentrated to dryness. The product was treated with acetic anhydride and pyridine at 50 °C overnight to give a crude triacetylated poly(**7**). The product was purified by silicagel column (Wacogel C-200; eluent: $CHCl_3$, and then 20% MeOH / $CHCl_3$), and by TLC (eluent: 10% MeOH / $CHCl_3$).give a triacetylated poly(**7**) (5.8 mg, 95%); ^{13}C-NMR: δ 100.8, 100.5, and 97.6 ppm (C_1 region).

Measurements. ^{1}H- and ^{13}C-NMR spectra were measured in chloroform-*d* with tetramethylsilane (TMS) as an internal standard using a Bruker ARX500 FT-NMR and a Bruker AC300 FT-NMR. Chemical shifts (δ) and coupling constants (*J*) are given in δ-values (ppm) and Hz, respectively. Optical rotations were measured using a JASCO Dip-1000 digital polarimeter. Infrared spectra were recorded with a Shimadzu FTIR-4000 spectrophotometer. X-ray diagrams were recorded with a Rigaku RINT 2200V. Molecular weight distributions of the substituted polymers were analyzed by gel permeation chromatography (GPC) in tetrahydrofuran. Calibration curves were obtained by using polystyrene standards (Shodex). A Waters universal liquid chromatograph injector (model U6K), a Waters solvent delivery system (model 6000A), a Waters refractive index detector (series R-400), a Waters absorbance detector (model 440), and Shodex columns (KF802 and KF803) were used. The flow rate was 1.0 mL / min.

REFERENCES

(1) Bochkov, A. F.; Zaikov, G. E. *Chemistry of the O-Glycosidic Bond-Formation and Cleavage*; Schuerch, C. trans eds., Pergamon Press: Oxford, 1979

(2) See, for example, Nevell, T. P.; Zeronian, S. H. Cellulose chemistry fundamentals in *Cellulose Chemistry and its Applications*; Nevell, T. P.; Zeronian, S. H. ed.: Ellis Horwood Limited, John Wiley & Sons: N. Y., 1985; pp 15 - 29.

(3) See books on cellulose: (a) Atalla, R. H. The Structures of Cellulose in *ACS Symposium Series 340*; Atalla, R. H. ed., American Chemical Society: Washington, DC 1987; pp 1 - 14. (b) Symposium on the Cellulose Structure and Its Characterization, and on the Biogenesis of Cellulose in *Cellulose and Wood — Chemistry and Technology, Proceedings of the Tenth Cellulose Conference*; Schuerch, C. ed., John Wiley & Sons, Inc.: N. Y., 1989; pp 39 - 322, 473 - 825.

(4) Schlubach, H. M.; Luhrs, *L. Ann* **1941**, *547*, 73.

(5) Kobayashi, S.; Kashiwa, K.;Kawasaki, T.;Shoda, S. *J. Am. Chem. Soc.* **1991**, *113*, 3079.

(6) (a) Sixou, P. *et al.* Cellulose Liquid Crystals in *Cellulose-Structure, Modification and Hydrolysis*; Young, R. A.; Rowell, R. M. eds. John Wiley & Sons: 1986; pp 203 - 261. (b) Siekmeyer, M. *et al.* Liquid Crystals in *Cellulose-Structure and Functional Aspects*; Kennedy, J. F.; Phillips, G. O.; Williams, P. A. eds.: Ellis Horwood: N. Y., pp 1989, 345.

(7) (a) Hesse, G.; Hagel, R. *Chromatographia* **1973**, *6*, 277. (b) Shibata, T.; Okamito, I.; Ishii, K. *J. Liq. Chromatog.* **1986**, *9*, 313. (c) Okamoto, Y.; Kawashima, M.; Hatada, K. *J. Am. Chem. Soc.* **1984**, *106*, 5357. (d) Shibata, T.; Sei, T.; Nishimura, H.; Deguchi, K. *Chromatographia* **1987**, *24*, 552.

(8) (a)Kamide, K.; Okajima, Matsui, T.; Kobayashi, H. *Polym. J.* **1983**, *15*, 309. (b) Okajima, K. Role of molecular charactersics on some physiological properties of cellulose derivatives in *Cellulose-Structure and Functional Aspects*; Kennedy, J. F.; Phillips, G. O.; William's, P. A. eds., Elise Horrid: N. Y., 1989; pp 439 - 446.

(9) (a) Matsuzaki, K.; Yamamoto, I.; Sato, T. *Makromol. Chem.* **1985**, *186*, 449. (b) Yamamoto, I.; Takayama, K.; Homma, K.; Gonda, T.; Matsuzaki, K.; Hatanaka, K.;

Uryu, T.; Yoshida, O.; Nakashima, H.; Yamamoto, N.; Kaneko, Y.; Mimura, T. *Carbohydr. Polym.* **1991**, *14*, 53.

(10) General reviews on polysaccharides synthesis: (a) Bochkov, A. F.; Zaikov, G. E. *Chemistry of the O-Glycosidic Bond-Formation and Cleavage*; Schuerch, C. trans eds., Pergamon Press: Oxford, 1979; pp 130 - 153. (b) Kochetkov, N. K. *Tetrahedron* **1987**, *43*, 2389. (c) Kochetkov, N. K. *Studies in Natural Products Chemistry, Vol. 14*, Elsevier Science B. V.: 1994; pp 201 - 266.

(11) Husemann, E.; Müller, G. J. M. *Makromol. Chem.* **1966**, *91*, 212.

(12) Hirano, S. *Agric. Biol. Chem.* **1973**, *37*, 187.

(13) (a) Micheel, F.; Brodde, O-E.; Reinking, K. *Liebigs Ann. Chem.* **1974**, 124. (b) Micheel, F.; Bordde, O-E. *ibid.* **1974**, 702. (c) Micheel, F.; Bordde, O-E. *ibid.* **1975**, 1107.

(14) Uryu, T.; Yamaguchi, C.; Morikawa, K.; Terui, K.; Kanai, T.; Matsuzaki, K. *Macromolecules* **1985**, *18*, 599.

(15) (a) Uryu, T.; Kitano, K.; Ito, K.; Yamanouchi, J.; Matsuzaki, K. *Macromolecules* **1981**, *14*, 1. (b) Uryu, T.; Yamanouchi, J.; Kato, T.; Higuchi, S.; Matsuzaki, K. *J. Am. Chem. Soc.* **1983**, *105*, 6865.

(16) Nakatsubo, F.; Takano, T.; Kawada, T.; Someya, H.; Harada, T; Shiraki, H.; Murakami, K. *Mem. Coll. Agric. Kyoto Univ.* **1985**, *127*, 37.

(17) (a) Takano, T.; Nakatsubo, F.; Murakami, K. *Cell. Chem. Technol.* **1988**, *22*, 135. (b) Takano, T.; Harada, Y.; Nakatsubo, F.; Murakami, K. *Cell. Chem. Technol.* **1990**, *24*, 333. (c) Takano, T.; Harada, Y.; Nakatsubo, F.; Murakami, K . *Mokuzai Gakkaishi* **1990**, *36*, 212.

(18) (a) Nishimura, T.; Takano, T.; Nakatsubo, F.; Murakami, K. *Mokuzai Gakkaishi* **1993**, *39*, 40. (b) Nishimura, T.; Nakatsubo, F.; Murakami, K. *Mokuzai Gakkaishi* **1994**, *40*, 44.

(19) (a) Kawada, T.; Nakatsubo, F.; Murakami, K. *Cell. Chem. Technol.* **1990**, *24*, 343. (b) Kawada, T.; Nakatsubo, F.; Murakami, K. *Mokuzai Gakkaishi* **1994**, *40*, 738. (c) Nishimura, T.; Nakatsubo, F.; Murakami, K. Abstracts of XVII Japanese Carbohydrate Symposium, 1995, 39.

(20) Deslongchamps P.; Mareau, C.; Frehel, D.; Atlani, P. *Can. J. Chem.* **1972**, *50*, 3402.

(21) Ichikawa, H.; Kobayashi, K.; Sumitomo, H.: *Carbohydr. Res.* **1988**, *179*, 315-320.

(22) Kobayashi, K.; Ishii, T.: Okada, M.; Schuerch, C: *Polymer J.* **1993**, *25*, 49-57.

(23) Micheel, F.; Kreutzer, U.; *Liebigs Ann. Chem.* **1969**, *722*, 228-231.

(24) Kamitakahara, H.; Nakatsubo, F.; Murakami, K. *Mokuzai Gakkaishi* **1994**, *40*, 302.

(25) Kamitakahara, H.; Nakatsubo, F. *Macromolecules* **1996**, *29*, 1119.

(26) Hashimoto, S.; Honda, T.; Ikegami, S.: *J. Chem. Sos., Chem. Commun.* **1989**, 685-687.

(27) Johansson, R.; Samuelsson, B.: *J. Chem.Soc., Perkin Trans. 1* **1984**, 2371-2374.

(28) Kamitakahara, H.; Nakatsubo, F.; Murakami, K. *Macromolecules* **1994**, *27*, 5937.

(29) Gagnaire, D. Y.; Taravel, F. R.; Vignon, M. R. *Carbohydr. Res.* **1976**, *51*,157.

(30) Malm, C. J.; Tangure, L. J.; Laird, B. C.; Smith, C. D. *J. Am. Chem. Soc.* **1953**, *75*, 80.

(31) Good, Jr.,F. J.; Schuerch, C. *Macromolecules* **1985**, *18*, 595.

(32) Zachoval, J.; Schuerch, C. *J. Am. Chem. Soc.* **1969**, *91*, 1165.

(33) Hall, H. K., Jr.; DeBlauwe, F.; Carr, L. J.;Rao, V. S.; Reddy, G. S. J. *J. Polym. Sci., Polym. Symp.* **1976**, *No 56*, 101.

(34) (a) Kochetkov, N. K.; Bochkov, A. F.; Yazlovertsky, I. G. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1966**, 1972. (b) Kochetkov, N. K.; Khorlin, A. Ya.; Bochkov, A. F.; Yazlovertsky, I. G. *Carbohydr. Res.* **1966**, *2*, 84. (c) Bochkov, A. F.; Yazlovertsky, I. G.; Kochetkov, N. K. *Izv. .Akad. Nauk SSSR, Ser. Khim.* **1968**, 1812. (d) Kochetkov, N. K.; Bochkov, A. F.; Yazlovertsky, I. G. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1968**, 1818. (e) Kochetkov, N. K.; Bochkov, A. F.; Yazlovertsky, I. G. *Carbohydr. Res.* **1969**, *9*, 49. (f) Bochkov, A. F.; Chernetsky, V. N.; Kochetkov, N. K. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1975**, 465. (g) Bochkov, A. F.; Obruchnikov, I. V.; Kochetkov, N. K. *Zh. Obshch. Khim.* **1972**, *42*, 2766. (h) Bochkov, A. F.; Obruchnikov, I. V.; Kochetkov, N. K. *Zh. Obshch. Khim.* **1974**, *44*, 1197. (i) Bochkov, A. F.; Chernetsky, V. N.; Kochetkov, N. K. *Carbohydr. Res.* **1975**, *43*, 35. (j) Bochkov, A. F.; Rodionov, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1976**, 2789.

(35) Bochkov, A. F.; Voznyi, Y. V.; Chernetskii, V. N.; Daxhunin, V. M.; Rodionov, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1975**, *45*, 420.

(36) Bochkov, A. F.; Rodionov, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1975**, *45*, 667.

(37) Colvin, E. W.; Purcell, T. A.; Rahael, R. A. *J. C. S. Chem. Comm.* **1972**, 1031.

(38) Paul, R.; Aderson, G. W. *J. Am. Chem. Soc.* **1960**, *82*, 4596.

(39) Ford, M. J.; Ley, S. V. *Synlett.* **1990**, 255.

(40) (a) Kutney, J. P.; Ratcliffe, A. H. *Syn. Commun.* **1975**, 47. (b) Kang, S-K.; Jeon, J-H.; Nam, K-S.; Park, C-H.; Lee, H-W. *Syn. Commun.* **1994**, *24*, 305.

(41) The author's initial plan was aimed at preparation of the 1,4-cyclic carbonate from compound **20**, which is also expected to be used as the starting monomer for polymerizations such as poly-α-amino acid synthesis from *N*-carboxy-α-amino acid anhydride.

(42) Nakatsubo, F.; Kamitakahara, H.; Hori, M. *J. Am. Chem. Soc.* **1996**, *118*, in press.

(43) Kamitakahara, H.; Nakatsubo, F. submitted to *Macromolecules*.

(44) Hall, L. D. Nuclear Magnetic Resonance in *Advances in Carbohydrate Chemistry Vol. 19* Wolfrom, M. L.; Tipson, R. S. ed., Academic Press: N. Y., London, 1964; pp 51 - 93.

(45) Pozsgay, V.; Nánási, P.; Neszmélyi, A. *Carbohydr. Res.* **1979**, *75*, 310.

(46) Private communication from Dr. Ken'ichi Takeo.

(47) See reviews on glycosylation: (a) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155. (b) Paulsen, H. *Chem. Soc. Rev.* **1984**, *13*, 15. (c) Schmidt, R. R. *Pure Appl. Chem.* **1989**, *61*, 1257. (d) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

(48) Burshtein, K. Y.; Fundiler, I. N.; Bochkov, A. F. *Tetrahedron* **1975**, *31*, 1303.

(49) Bochkov, A. F. Dr. Sci. dissertation N. D. Zelinsk Institute of Organic Chemistry, Moscow, 1975.; Obruchnikov, I. V.; Kochetkov, N. K.

(50) Bochkov, A. F.; Rodionov, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1975**, 667.

(51) (a) Atalla, R. H.; Ellis, J. D.; Schroeder, L. R. *J. Wood Chem. Technol.* **1984**, *4*, 465. (b) Isogai, A.; Usuda, M. *Mokuzai Gakkaishi* **1991**, *37*,339.

(52) Jones, D. W. X-ray and electron diffraction in *Cellulose and Cellulose Derivatives Part IV*; Bikales, N. M.; Segal, L. ed., Wiley-Interscience: N. Y., 1971; pp 117 - 180.

(53) Mathers, D. S.; Robertson, G.J.: *J. Chem. Soc.* **1933**, 696-698.

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